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Evaluation of Military Field-Water Quality

Volume 6. Infectious Organisms of Military Concern Associated with Nonconsumptive Exposure: Assessment of Health Risks and Recommendations for Establishing Related Standards

R. C. Cooper
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February 1986

Lawrence Livermore National Laboratory

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This study is an assessment of the risk of illness due to exposure to water-related (i.e., water-based, water-washed) infectious organisms. The organisms under consideration are *Aeromonas* spp., *Leptospira* spp., *Pseudomonas* spp., *Staphylococcus* spp., non-*cholerae Vibrio* spp., *Acanthamoeba* spp., *Balantidium coli*, *Naegleria* spp., *Ascaris lumbricoides*, *Dracunculus medinensis*, *Schistosoma* spp., and the agents responsible for cercarial dermatitis (i.e., *Trichobilharzia*, *Gigantobilharzia*, and *Austrobilharzia*). Evaluation of the risk to disease associated with the above pathogens requires information in specific areas such as dose response, concentration of agents in the environment, and environmental persistence. The existing body of knowledge concerning these agents ranges from speculation to established fact. Unfortunately, areas of information critical to risk assessment are frequently unavailable. Because of this lack of data, the risk assessment presented is semiquantitative and limited to the presentation of an environmental classification

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scheme that provides a relative comparison of the risk of illness associated with the pathogens, based on their key environmental features and control strategies.

This report is the sixth volume of a nine-volume study entitled Evaluation of Military Field-Water Quality. Titles of the other volumes are as follows: Vol. 1, Executive Summary; Vol. 2, Constituents of Military Concern from Natural and Anthropogenic Sources; Vol. 3, Opportunity Poisons; Vol. 4, Health Criteria and Recommendations for Standards; Vol. 5, Infectious Organisms of Military Concern Associated with Consumption: Assessment of Health Risks, and Recommendations for Establishing Related Standards; Vol. 7, Performance Evaluation of the 600-GPH Reverse Osmosis Water Purification Unit (ROWPU): Reverse Osmosis (RO) Components; Vol. 8, Performance of Mobile Water Purification Unit (MWPU) and Pretreatment Components of the 600-GPH Reverse Osmosis Water Purification Unit (ROWPU) and Consideration of Reverse Osmosis (RO) Bypass, Potable-Water Disinfection, and Water-Quality Analysis Techniques; and Vol. 9, Data for Assessing Health Risks in Potential Theaters of Operation for U.S. Military Forces.

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Evaluation of Military Field-Water Quality

Volume 6. Infectious Organisms of Military Concern Associated with Nonconsumptive Exposure: Assessment of Health Risks and Recommendations for Establishing Related Standards

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Principal Investigators at Lawrence Livermore National Laboratory:
L. R. Anspaugh, J. I. Daniels, and D. W. Layton

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The findings of this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

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FOREWORD

This report is the sixth volume of a nine-volume study entitled Evaluation of Military Field-Water Quality. Titles of the other volumes are as follows: Vol. 1, Executive Summary; Vol. 2, Constituents of Military Concern from Natural and Anthropogenic Sources; Vol. 3, Opportunity Poisons; Vol. 4, Health Criteria and Recommendations for Standards; Vol. 5, Infectious Organisms of Military Concern Associated with Consumption: Assessment of Health Risks, and Recommendations for Establishing Related Standards; Vol. 7, Performance Evaluation of the 600-GPH Reverse Osmosis Water Purification Unit (ROWPU): Reverse Osmosis (RO) Components; Vol. 8, Performance of Mobile Water Purification Unit (MWPU) and Pretreatment Components of the 600-GPH Reverse Osmosis Water Purification Unit (ROWPU) and Consideration of Reverse Osmosis (RO) Bypass, Potable-Water Disinfection, and Water-Quality Analysis Techniques; and Vol. 9, Data for Assessing Health Risks in Potential Theaters of Operation for U.S. Military Forces.

The nine volumes of this study contain a comprehensive assessment of the chemical, radiological, and biological constituents of field-water supplies that could pose health risks to military personnel as well as a detailed evaluation of the field-water-treatment capability of the U.S. Armed Forces. The scientific expertise for performing the analyses in this study came from the University of California Lawrence Livermore National Laboratory (LLNL) in Livermore, CA; the University of California campuses located in Berkeley (UCB) and Davis (UCD), CA; the University of Illinois campus in Champaign-Urbana, IL; and the consulting firms of IWG Corporation in San Diego, CA, and V.J. Ciccone & Associates (VJCA), Inc., in Woodbridge, VA. Additionally a Department of Defense (DoD) Multiservice Steering Group (MSG), consisting of both military and civilian representatives from the Armed Forces of the United States (Army, Navy, Air Force, and Marines), as well as representatives from the U.S. Department of Defense, and the U.S. Environmental Protection Agency provided guidance, and critical reviews to the researchers. The reports addressing chemical, radiological, and biological constituents of field-water supplies were also reviewed by scientists at Oak Ridge National Laboratory in Oak Ridge, TN, at the request of the U.S. Army. Furthermore, personnel at several research laboratories, military installations, and agencies of the U.S. Army and the other Armed Forces provided technical assistance and information to the researchers on topics related to field water and the U.S. military community.

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Volume 6. Infectious Organisms of Military Concern Associated with Nonconcumptive Exposure: Assessment of Health Risks and Recommendations for Establishing Related Standards

ABSTRACT

This study is an assessment of the risk of illness due to exposure to water-related (i.e., water-based, water-washed) infectious organisms. The organisms under consideration are Aeromonas spp., Leptospira spp., Pseudomonas spp., Staphylococcus spp., non-cholerae Vibrio spp., Acanthamoeba spp., Balantidium coli, Naegleria spp., Ascaris lumbricoides, Dracunculus medinensis, Schistosoma spp., and the agents responsible for cercarial dermatitis (i.e., Trichobilharzia, Gigantobilharzia, and Austrobilharzia). Evaluation of the risk to disease associated with the above pathogens requires information in specific areas such as dose response, concentration of agents in the environment, and environmental persistence. The existing body of knowledge concerning these agents ranges from speculation to established fact. Unfortunately, areas of information critical to risk assessment are frequently unavailable. Because of this lack of data, the risk assessment presented is semiquantitative and limited to the presentation of an environmental classification scheme that provides a relative comparison of the risk of illness associated with the pathogens, based on their key environmental features and control strategies.

CHAPTER 1. INTRODUCTION

This study, an assessment of the risk of illness resulting from nonconsumptive exposure to water-related infectious organisms, is Volume 6 of the nine-volume series, Evaluation of Military Field-Water Quality. The assessment is based on data available in the published literature, and a list of the organisms addressed in this volume is shown in Table 1. (A companion report, Volume 5 of this series, is concerned with infectious organisms and consumption of field water; it also includes the screening procedure that we used to select the organisms addressed in both Volumes 5 and 6.)

Volume 6 contains 15 chapters, each with a separate list of references. Following the introductory chapter (Chapter 1), Chapters 2 through 13 describe the environmental properties of a specific pathogen or group of pathogens, as well as the epidemiology and control of diseases associated with these infectious organisms. Grouped by biological class of pathogen, these chapters are arranged as follows: bacteria (2 through 6), protozoa (7 through 9), and helminths (10 through 13). In each of these chapters, we emphasize (1) the occurrence and concentration of the pathogen in the environment, dose-response relationships, and indicator-organism/pathogen relationships; and (2) the complex (and sometimes contradictory) evidence for the key environmental factors (i.e., latency, infectivity, environmental persistence, and median infective dose). Chapter 14 is a discussion of the health risks associated with the organisms shown in Table 1. This risk assessment is semiquantitative and limited to a presentation of an environmental classification scheme that enables relative comparison of the risk of illness associated with the pathogens, based on their key environmental features and control strategies. In Chapter 15, we discuss the uncertainties that became evident in our research, and we make recommendations for areas of further study.

WATER-RELATED DISEASES: SCREENING

As mentioned, the screening procedure used to select the organisms identified for investigation within this volume is discussed in Volume 5.[1] In general, the screening procedure involved the identification of all water-related diseases, as well as the accumulation of data on their geographic distribution and rates of morbidity and mortality. In instances where data were found, the disease and organism were then listed for further study (Table 2). The risk assessment and discussion of environmental factors

Table 1. Water-related pathogens selected for review.

Bacteria	Protozoa	Helminths
Non-cholerae Vibrio spp.	Acanthamoeba spp.	Dracunculus medinensis
Pseudomonas spp.	Naegleria spp.	Ascaris lumbricoides
Staphylococcus spp.	Balantidium spp.	Schistosoma spp.
Leptospira spp.		Trichobilharzia spp.
Aeromonas spp.		Gigantobilharzia spp.
		Austrobilharzia spp.

Table 2. Water-related diseases.

Infectious organisms	Description
Bacteria	Bacillary dysentery (Shigella spp.)*
	Cholera (Vibrio cholerae)*
	Diarrhea (Campylobacter)*
	Diarrhea (Escherichia coli)*
	Leptospirosis (Leptospira spp.)
	Salmonellosis (Salmonella spp.)*
	Typhoid fever (Salmonella typhi)*
	Skin infections (Pseudomonas spp., Staphylococcus spp., Aeromonas spp., and non-cholerae Vibrio spp.)
	Yersiniosis (Yersinia spp.)*
Virus	Enteroviruses*
	Gastroenteritis, Norwalk agent, and rotavirus*
	Hepatitis A (hepatitis virus)
Parasite	Acanthamebiasis (Acanthamoeba spp.)
	Amebic dysentery (Entamoeba histolytica)*
	Ascariasis (Ascaris lumbricoides)
	Balantidium dysentery (Balantidium coli)
	Dracontiasis (Dracunculus medinensis)
	Giardiasis (Giardia lamblia)*
	Meningoencephalitis (Naegleria spp. and Acanthamoeba spp.)
	Schistosomiasis (Schistosoma spp.)
	Cercarial dermatitis (Trichobilharzia spp., Gigantobilharzia spp., and Austrobilharzia spp.)

* Indicates that the risk assessment and data base are contained in Ref. 1.

for the diseases and organisms marked with an asterisk "*" in Table 2 can be found in the main text and appendices of Volume 5.[1] The remaining diseases and organisms listed in Table 2 are addressed in this volume.

As shown in Table 3, the water-related organisms can be classified by their route of transmission. In general, this report addresses those organisms that are classified as water-based and water-washed; Volume 5[1] addresses the bacterial, viral, and parasitic diseases classified as waterborne.

DATA-BASE DEVELOPMENT

To achieve an adequate literature review, a systematic work plan was constructed as shown in Fig. 1. The emphasis of the literature review primarily was on recent literature (after 1970), and our goal was to ultimately retain only data of value to risk assessment.

Information on the criteria shown in Table 4, for each disease agent, was derived from a study of basic reference works, recent review articles, the periodical literature, and an overview of related subjects in published collections of journal abstracts. The review involved the following sequence:

- Identification of relevant criteria for infectious agents;
- Assembly of bibliographical references;
- Acquisition of the pertinent literature;
- Extraction of relevant information:
- Development of a computerized index and data base; and
- Evaluation of the data.

From Fig. 1, it can be seen that the generation of the data base was cyclical (i.e., it was continually updated, and it includes most of the current literature pertinent to the investigation). It is estimated that approximately 1300 relevant abstracts were scanned for selection of appropriate articles. The WRC Information* and Current Contents† were reviewed for pertinent material. In addition to the manual methods of literature review,

* WRC Information is the weekly journal of the Water Research Center, Medmenham, Marlow, Bucks SL72HD, UK.

† Current Contents: the periodical covering life sciences and agriculture, biology, and environmental sciences, is published by the Institute for Scientific Information, Philadelphia, PA 19104.

Table 3. Water-related pathogens and routes of transmission.

Pathogen	Waterborne[a]	Water-washed[b]	Water-based[c]
Bacteria:			
Non-cholerae Vibrio spp.	--	X	--
Pseudomonas spp.	--	X	--
Staphylococcus spp.	--	X	--
Leptospira spp.	X	--	--
Aeromonas spp.	--	X	--
Protozoa:			
Acanthamoeba spp.	--	X	--
Naegleria spp.	--	X	--
Balantidium spp.	X	X	--
Helminths:			
Dracunculus medinensis	--	--	X
Ascaris lumbricoides	--	X	--
Schistosoma spp.	--	--	X
Agents of cercarial dermatitis	--	--	X

[a] Waterborne: fecal-oral infections via water.

[b] Water-washed: fecal-oral infections via direct contact; skin and eye infections.

[c] Water-based: helminth penetrates skin; helminth ingested.

the Medline and Aqualine computer data bases were used to retrieve relevant abstracts. Medline corresponds to three printed indices: Index Medicus, Index to Dental Literature, and International Nursing Index, covering over 3000 international journals. Aqualine provides access to information on every aspect of water, wastewater, and the aquatic environment, citing over 400 worldwide periodicals, research reports, books, etc. From the aforementioned list of abstracts, approximately 400 articles were retrieved, read, and included in the data base. From the 400 articles, books, reports, proceedings, and other sources, approximately 350 were chosen for reference and inclusion in this report. It is our belief that most, if not all, of the pertinent literature retrievable by feasible methods has been identified.

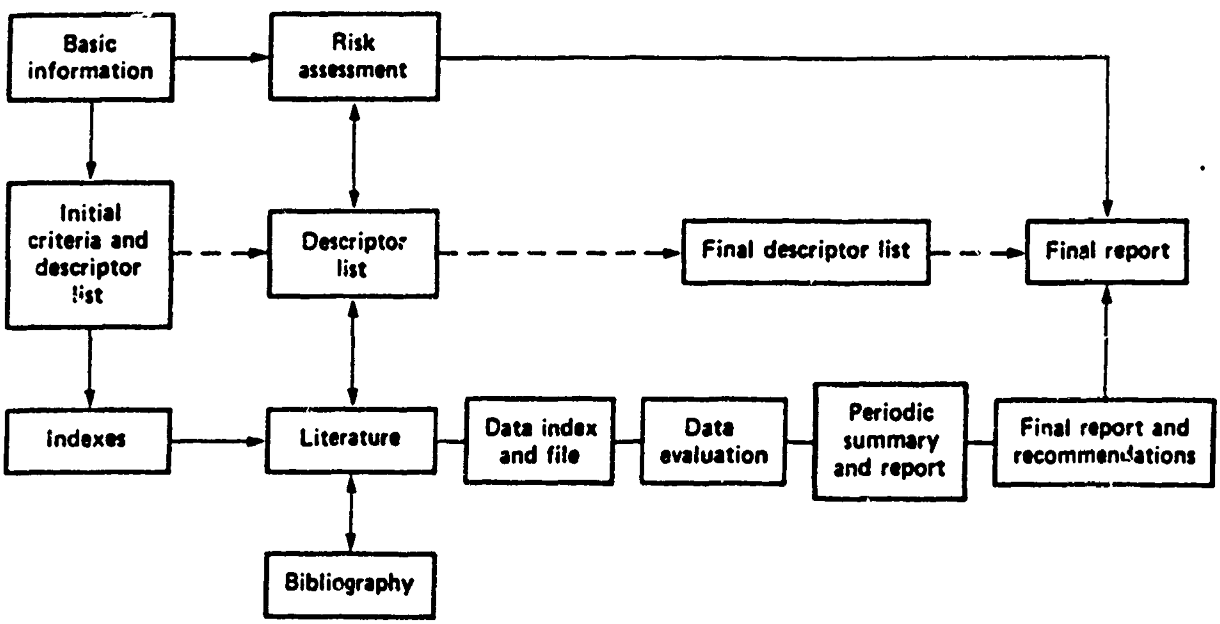

Figure 1. General data-base development plan.

Table 4. Infectious-agent criteria.

Criteria	Content
Occurrence	Worldwide distribution of disease
Latency	Incubation period
Persistence	Survival time in final infective stage
Infective dose	Dose data
Attack rate	Rate of new cases of a specific disease
Multiplication	Multiplication outside human host
Route of transmission	Waterborne, water-washed, water-based
Disinfectant resistance	In disinfected water
Indicator-organism/pathogen relationship	Coliform numbers relative to pathogen concentration
Prevalence	Infection rate

Data Base

A command-driven, relational data-base system was developed for our literature search. The dBase III system, developed by Ashton-Tate,[2] was the data-management software used for this task. The software and manuals are readily available. Over 400 articles are included within this data base. The data-base files, together with the dBase III software, allow easy access and retrieval of key criteria listed in Table 4. A complete sample printout from the data base for one article is shown in Table 5. The data-base key is shown in Table 6.

Table 5. Sample data-base printout.

```
RECORD # 00020
REFCODE  : Craun 78 :
ABSTRACT : Data are presented on waterborne outbreaks of         :
ABS1     : giardiasis affecting travelers to foreign countries,  :
ABS2     : esp. the USSR, and residents in the US. 23 outbreaks  :
ABS3     : on the US reported since 1965. Usually in mountainous :
ABS4     : areas of the US: New England, the Pacific Northwest,  :
ABS5     : and the Rocky mountains. Generally involves small     :
ABS6     : municipal systems, or semi-public systems, or         :
ABS7     : untreated water.  Most come from consuming            :
ABS8     : untreated or only chlorine treated surface water.     :
ABS9     : Negative results of coliform tests do not provide a   :
ABS10    : guarantee that water is free of Giardia cysts. Attack :
ABS11    : rate is of visitors to Leninrad who drank tap water. In :
ABS12    : Colorado mountain streams, there are up to 500 fecal  :
ABS13    : coliforms /100ml. This figure may be low. In the      :
ABS14    : Rome, N.Y. outbreak, with 4800 cases, one cyst was    :
ABS15    : isolated from 1 million liters of raw water from the  :
ABS16    : plant intake.                                         :

RECORD # 00020
REFCODE  : Craun 78 :
SEQNUM   :2:
CITATOR  :pgb:
AUTHOR:LST:Craun G.F.

:
TITLE      :"Waterborne Outbreaks of Giardiasis" in Jakubowski &
Hoff, eds., Waterborne Transmission of Giardiasis: Proceedings of a
Symposium. US EPA

:
CITATION   :EPA Office of R&D, Env. Research Center, Cincinnati, Ohio
:
YEAR       :(1978) :
KEY:WORD :Giardiasis, chlorination, filtration, outbreak, coliform
count. Giardia lamblia, giardiasis
:
LOCATION :worLdwide      :
LATENCY  :Y:
ATKRT    :Y:
PESIST   :Y:
MID      :N:
PROPHO   :Y:

RECORD # 00020
CONENV   :fresh   :
DISINTYPE :       :

RECORD # 00020
REFCODE     : Craun78  :
LAT:MAX     : 56       :
LAT:MIN     : 7        :
LAT:AVE     :          :
ATKRTEMAX   : 330      :
ATKRTEMIN   : 230      :
ATKRTEAVE   :          :
PESIST      :2 to 3 months in host.

:
MULTOUTHST  :no  :
MIDMAX      :          :
MIDMIN      :          :
MIDAVE      :          :
RTETRANS    :fecal-oral   :
SIGIMMUN    :?  :
PROPHO      :yes  :
PROPHOTYPE  :Filter water in addition to chlorination of surface
water, preceded by sedimentation or coagulation.
:
OPPORTUNE  :   :
OPTENVTEMP :low    :
OPTENVSAL  :   :

RECORD # 00020
OPTENVPH    :   :
ENVRANGE    :   :
DOSE1       :   :
DOSE2       :   :
DOSE3       :   :
DOSE4       :   :
DOSE5       :   :
RESP1       :      :
RESP2       :      :
RESP3       :      :
RESP4       :      :
RESP5       :      :
INDPATH     :Negative results of coliform tests don't provide
assurance that water is free of Giardia cysts.  Positive results often
correlate with outbreaks.
```

Table 6. Data-base key.

Field	Item
REFCODE	reference code
SEQNUM	sequence number
CITATOR	initials of citator
AUTHOR:LST	list of authors
TITLE	title of article
CITATION	journal, book, report
YEAR	year of publication
KEY:WORD	list of key words
LOCATION	country, state, city of research
LATENCY	information in article, yes or no, Y/N
ATKRT	attack rate information in article, Y/N
PESIST	persistence information in article, Y/N
MID	median infective-dose information, Y/N
PROPHO	prophylactic information, Y/N
CONENV	type of water in which the organism is found
DISINTYPE	type of disinfectant
ABSTRACT	citator abstract
LAT:MAX, LAT:MIN, LAT:AVE	maximum, minimum, average latency data
ATKRTEMAX, MIN, AVE	maximum, minimum, average attack rates
MULTOUTHST	multiplication outside host
MIDMAX, MIDMIN, MIDAVE	median effective-dose data
RTETRANS	route of transmission
SIGIMMUN	immunity data
PROPHOTYPE	prophylactic type
OPPORTUNE	opportunistic organism
OPTENVTEMP	optimum environmental temperature
OPTENVSAL	optimum environmental salinity
OPTENVPH	optimum environmental pH
ENVRANGE	description of environmental conditions of research
DOSE1	disinfectant dose
RESP1	organism response
INPATH	indicator pathogen relationship

REFERENCES

1. Cooper, R. C., A. W. Olivieri, R. E. Danielson, and P. G. Badger, Evaluation of Military Field-Water Quality. Volume 5. Infectious Organisms of Military Concern Associated with Consumption: Assessment of Health Risks, and Recommendations for Establishing Related Standards, Lawrence Livermore National Laboratory, Livermore, CA, UCRL-21008, Vol. 5 (1986).

2. Ashton-Tate, dBase III, Culver City, CA (1985).

CHAPTER 2. BACTERIA: Aeromonas spp.

ETIOLOGY AND CLINICAL DISEASE

The bacteria of the genus Aeromonas are Gram-negative, aerobic, short rods common to the aquatic environment.[1] Aeromonas have only recently been recognized as a primary pathogen to man, mainly as a cause of gastroenteritis, but also as a cause of wound infections.[2-4] Aeromonas have also been found to infect major organ systems in immunocompromised individuals.[3] Previously, Aeromonas were thought to be an infective agent only in reptiles and birds ("red leg" in frogs, "black rot" in hens' eggs).[1,5] Most of the isolates from human infections have been Aeromonas hydrophila or A. sobria, although A. punctata have also been isolated from human infections.[5-7] These infections occur most often in healthy individuals who have ingested the A. hydrophila organism or who have suffered a water- or soil-related trauma.[2,3] Aeromonas are not considered a common inhabitant of the human intestine, although they have been isolated from the guts of even healthy persons.[2]

Gastrointestinal involvement from ingesting food or water contaminated with Aeromonas spp. presents itself as an enteric fever or cholera-like symptoms.[5,8-11] Such gastrointestinal infections by Aeromonas are usually self-limiting, lasting only a few days.[3] Recently, a cholera-like enterotoxin has been identified from A. hydrophila and A. sobria.[6,8-10,12,13] This toxin has been shown to produce a threefold increase in the level of cAMP* in the human gut.[13] Campbell et al. found that this toxin, from A. hydrophila, cross-reacted with antisera for cholera toxin.[12] This organism has also shown the ability to cross the gut-blood barrier, enter the circulatory system, and disseminate throughout the host.[3]

Aeromonas spp. have been isolated from the pus of wound infections.[2-5] Wound infection sites become swollen and painful, and the patient suffers from fever and chills.[2] Introduction of Aeromonas spp. by trauma may lead to septicemia and the involvement of major organs, and secondary infections such as endocarditis,[3] meningitis,[3,14] and pneumonia.[4] This organism flourishes especially well in muscle tissue.[3,4,15] Aeromonas spp. are sensitive to the antibiotics cephalosporin, gentamycin, kanamycin, chloramphenicol, and tetracycline, and they are resistant to penicillin and

* cAMP = cyclic adenosine monophosphate (monophosphate form of adenosine triphosphate, ATP).

ampicillin (although some environmental strains have been found to be susceptible to ampicillin).[2-4,15,16] Carbenicillin has also been shown to be effective in treating infections produced by Aeromonas spp.[3]

OCCURRENCE

Aeromonas spp. are ubiquitous bacteria found worldwide in fresh and salt waters, sewage, and soil.[3,5,17-20] Aeromonas spp. are opportunistic for wound infections, but the severity of the infection depends upon the concentration of the Aeromonas spp. organisms in the water or soil that contaminates the wound.

Clark et al.[21] reported the occurrence of Aeromonas spp. in raw-water supplies as well as treated water (see Environmental Concentration section). Surveys of diarrhea patients living in low-economic areas in a developed country revealed a 12 to 18% population prevalence rate.[17,22] A survey of 39 Peace Corps volunteers in Thailand found that within 5 wk of arrival, 31% (12/39) had developed diarrhea associated with A. hydrophila (the most common pathogen isolated).[23] Stephan et al. reported a wide variety of clinical symptoms due to Aeromonas spp. (infections and diarrhea) from persons in India whose occupations included extensive contact with water (i.e., wading in wet fields, fishing, etc.).[5]

Aeromonas hydrophila have been associated more with disease in developed western countries, whereas A. sobria appear to be isolated with greater frequency in the Far East.[6] Human carrier frequencies in feces have been reported to be 0.2 to 0.7% in normal individuals, with one study reporting a frequency of 3.2% in nondiarrheal patients.[24] Burke et al. reported that the incidence of gastroenteritis due to Aeromonas peaked in Australia during the summer months.[25] This increase in numbers of cases of gastroenteritis coincided with the observed increase of Aeromonas spp. in the drinking-water supply.

RESERVOIR

Aeromonas spp. are ubiquitous in fresh and marine waters and found in moist soils worldwide.[24]

MODE OF TRANSMISSION

Aeromonas spp. gain access to the host by either direct contact or ingestion of water or foodstuffs in which the bacteria are present.[7,16,18,26,27]

SUSCEPTIBILITY AND RESISTANCE

No information was identified in our search of the literature concerning the susceptibility and resistance of the human host against Aeromonas spp., although it appears that there is universal susceptibility whenever a sufficient number of organisms is encountered.[2-7,10,12,13,17,18]

ENVIRONMENTAL PERSISTENCE

As previously stated, Aeromonas spp. are ubiquitous in moist soil and in fresh and salt waters. These organisms survive in a wide variety of environmental conditions, as illustrated in Table 1. Optimum growth temperature ranges from 20° to 30°C for Aeromonas.[11] In a recent survey, Rouf et al.[29] found that 80% of 33 strains of Aeromonas were mesophilic (optimum temperature: 20 to 35°C), whereas 20% were reported to be psychrophilic (optimum temperature: 15 to 20°C).

Slotnick[14] stated that Aeromonas is very sensitive to drying on surfaces (Table 1). When applied to a bench top directly, Aeromonas died off completely within 4 h. On dry mammalian skin (rabbit), Aeromonas survival varied from 2 to 48 h.

McFeters et al. compared the survival of Aeromonas with that of other waterborne bacterial pathogens and indicators in well water.[30] Aeromonas were found to survive the longest at pH 7.8 and at temperatures from 9 to 13°C. The other organisms compared to Aeromonas with respect to survival under these conditions and their comparative survivability were as follows: Aeromonas > Shigella > fecal Streptococcus > coliforms and Salmonella spp. > Streptococcus equinas > Vibrio cholerae > Salmonella typhi > Streptococcus bovis > Salmonella enteritidis.

Hanson et al. reported a decline in the number of Aeromonas organisms in a lake over a distance of 2 km from the contamination source.[2] However, the number of organisms was reduced by only a factor of 2.5 logarithms over this distance. Hazen and Esch have shown that A. hydrophila growth is enhanced in river water by the presence of chlorophyll A, with an increase in dissolved oxygen and phosphate and a lowered redox potential.[31] This finding, however, contradicts the earlier work of Hazen et al.,[28] which found Aeromonas in polluted rivers (eutrophic conditions, low oxygen). Hazen et al. also conducted a survey of 143 sites in the United States for the presence of Aeromonas spp.[28] Of the 143 sites sampled, 135 (92%) were found to harbor Aeromonas spp. The only environments found lacking in Aeromonas were hypersaline lakes (>100 parts per thousand), geothermal springs (> 45°C), and extremely polluted rivers. The ranges

Table 1. Environmental persistence of Aeromonas spp.

Environmental source	Temperature (°C)	Salinity (o/oo)	pH	Turbidity (JTU)	Time (h)	Survival	Ref.
River	4	-	-	-	48	99.9[a]	11
River	25	-	-	-	48	0[a]	11
Variety of aquatic habitats	4-<45	<100	5-9	0-395	-	(+)[b]	28
Drinking water[c]	>14.5	-	-	-	-	(+)[b]	25
Drinking water[d]	14-27	-	-	-	-	(+)[b]	27
Surfaces:							
Bench top	-	-	-	-	2-4	0[e]	14
Damp towel	-	-	-	-	24[f]	0[e]	14
Damp towel	-	-	-	-	2 wk[g]	0[e]	14
Rabbit skin	-	-	-	-	2-48	0[e]	14
Rabbit skin	4-40	-	-	-	-	(+)[b]	14
Estuary	20-29	0.7-20.1	-	-	-	(+)[b]	19

[a] Percent die-off of bacteria.

[b] (+) = Aeromonas spp. present in environments within the ranges of the variables listed.

[c] Treated drinking water, reservoirs, and water-distribution systems.

[d] Unchlorinated tap water.

[e] No longer detectable.

[f] Damp paper towel allowed to dry.

[g] Damp paper towel not allowed to dry.

of environmental conditions for Aeromonas found by this survey are presented in Table 1. Although it is generally believed that this organism is a freshwater bacteria, the greatest concentrations were found in marine waters (see Environmental Concentration section). Kaper et al. found Aeromonas to be ubiquitous in estuarine environments.[19]

DOSE RESPONSE

Morgan et al. recently demonstrated the dose response for Aeromonas enteropathogenicity (Table 2).[18] Aeromonas hydrophila was fed to 57 individuals at doses

Table 2. Dose response for Aeromonas hydrophila.

Dose (No. of organisms)	Latency (h)	Response (%)[a]	Ref.
10^9	24	1.7(1/57)[b]	18
10^8	-	0(0.57)[b]	18
10^7	24	1.7(1/57)[b]	18
10^6	-	0(0/57)[b]	18
10^5	-	0(0/57)[b]	18
10^4	-	0(0/57)[b]	18
<500[c]	24	100(1/1)[d]	2
<1500[e]	-	100(1/1)[d]	4

[a] $\text{Percentage} = 100 \times \frac{\text{no. individuals responding}}{\text{no. individuals exposed}}$

[b] Response = gastroenteritis resulting in diarrhea.

[c] Dose ≤ 500 organisms/100 mL of lake water (i.e., 5000 organisms/L at site of trauma.

[d] Wound infection.

[e] Dose ≤ 1500 colony-forming units (cfu)/g of fish, subsequently transferred by contaminated hand to a dialysis needle, which was inserted into a dialysis patient (i.e., immunocompromised host).

between 10^4 and 10^9 organisms, with only one individual responding with gastroenteritis at doses of 10^7 and 10^9 organisms. Doses have been estimated for wound infections based on the environmental exposure concentration of Aeromonas (Table 2).[2,4] For example, Hanson et al.[2] measured approximately 500 A. hydrophila organisms per 100 mL at a freshwater site of an accident in which a wound infection was acquired within 24 h of exposure. Farrington and Gray described an infection from a dialysis needle contaminated from hands that were preparing a fish contaminated with about 1500 colony-forming units (cfu) of A. hydrophila organisms per gram of fish.[4]

LATENCY

The latency to onset of clinical symptomology for Aeromonas is presented in Table 2. For gastroenteritis and wound infections, the latency is about 24 h from exposure to onset of disease.[2,18]

DISINFECTANTS

Aeromonas spp. appear to be fairly resistant to chlorine, as they have been recovered from recently disinfected drinking water.[25,27] One study[25] comparing chlorine levels in drinking water with Aeromonas concentration revealed that Aeromonas are capable of reproducing at low levels of residual chlorine. A fourfold rise in Aeromonas concentration was observed when levels of free-available chlorine were less than or equal to 3 mg/L. However, most drinking-water chlorine concentrations were measured at 0.3 mg/L, in which Aeromonas were consistently recovered.

MONITORING METHODS

There is no standard methodology for the recovery of Aeromonas presented in Standard Methods for the Examination of Water and Wastewater, 16th ed.[32] Most often this organism may be isolated and enumerated using membrane filtration. These filters are incubated on pads soaked with Rimler-Shotts medium (commercially available).[28] Aeromonas spp. appear yellow on this medium.

Other methods for isolation include the use of standard laboratory media: blood agar, enteric differential agars, and tryptic digest broths.[24] Abeyta et al. have suggested that tryptic soy broth with ampicillin (TSBA) be employed as an enrichment step for Aeromonas spp.[9]; however, as previously stated, ampicillin has been found to be inhibitory to some environmental isolates.[16] Recently, Altorfer et al. have developed a selective medium for Aeromonas spp.[33] This agar-based medium includes Cefsulodin-Irgasan- Novobiocin (CIN), and the plates are incubated at 25°C for best recovery.

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

In general, there is no relationship between established indicators and the occurrence of Aeromonas spp.[19,20,26,27] The absence of any correlation between indicators and Aeromonas spp. is probably the result of the ubiquitous nature of the Aeromonas genera in the aquatic environment. Some of these data have been summarized and are shown in Table 3. Not all environmental isolates are pathogenic, however. A summary of the percentage of isolates found to be pathogenic for various studies is shown in Table 4.

There have been some attempts to use Aeromonas as an indicator of water quality. Kaper et al. reported that the presence of Aeromonas spp. in the Chesapeake Bay was a good indicator of eutrophication due to its ability to flourish in low-dissolved-oxygen (DO), nutrient-rich environments.[19] In Denmark, Larsen and Willeberg[20] found that A. hydrophila was a much better indicator of fecal pollution of bathing beaches because it can survive better in the marine environment. However, because these organisms are

Table 3. Indicator-organism/pathogen relationship for Aeromonas.

	Indicator organisms					
Aeromonas[a]	TC[b]	FC[c]	E. coli	Environment	Location	Ref.
40	-	1	-	Lake water	U.S.	2
8	-	1	-	Lake water	U.S.	2
5	-	1	-	Lake water	U.S.	2
2	1	-	1	Raw water	Australia	25
3	1	-	1	Reservoirs	Australia	25
3	1	-	1	Tap water	Australia	25
3	-	1	-	Raw water	Canada	21
3	-	1	-	Well water	Canada	21
1	-	1	-	Lake water	Canada	21
2	-	1	-	Mixed source	Canada	21
16	-	1	-	New mains	Canada	21
1-10	-	1	-	River water	U.S.	31
(+)[d]	-	-	-	Oyster beds	U.S.	26
(+)[d]	-	-	-	Reservoirs	Australia	27
(+)[d]	-	-	-	Estuary	U.S.	19
(+)[d]	-	-	-	Bathing beaches	Denmark	20

[a] Unless otherwise stated, numbers are expressed as ratios of pathogen to indicator.

[b] Total coliforms.

[c] Fecal coliforms.

[d] (+) indicates presence of Aeromonas spp., and here was no correlation found with indicators.

Table 4. Percent of pathogenic isolates for Aeromonas.

Pathogenic (%)	Source of pathogenesis	Environment	Location	Ref.
80	Hemolysin	Shellfish beds	U.S.	9
4.5	Cholera toxin	-	Japan	10
70	Enterotoxin	Drinking-water reservoirs	Australia	25
91	Enterotoxin	Fecal isolates	Australia	25
70	Enterotoxin	Estuary	U.S.	19

apparently ubiquitous, one must know the background levels. Larsen and Willeberg state that a concentration of A. hydrophila in recreational water of 500 organisms/100 mL puts those exposed at risk of infection.[20] As will be shown in the next section, a review of the literature on concentrations of Aeromonas in the environment indicates that this level is frequently exceeded.

ENVIRONMENTAL CONCENTRATION

Table 5 contains data related to the observed environmental concentrations of Aeromonas spp. It is obvious that this organism has a wide distribution throughout freshwater and marine-water environments. Two separate studies[3,25] have revealed that Aeromonas can be isolated frequently from water-distribution systems. Burke et al. have shown that major increases of Aeromonas in water-distribution systems in Australia result in the increase in gastroenteritis caused by Aeromonas.[25]

Table 5. Environmental concentration of *Aeromonas* spp.

Organism concentration	Environment	Location	Ref.
3-2400/100 mL	Brackish water	U.S.	9
3-4600/g oyster	Shellfish bed	U.S.	9
130 cfu/mL[a]	Fresh water	U.S.	28
746 cfu/mL[a]	Marine waters	U.S.	28
0.1-100 cfu/mL	River	U.S.	31
500 cfu/100 mL	Bathing beaches	Denmark	20
10^5/100 mL	Ditch	U.S.	2
10^2/100 mL	Lake	U.S.	2
10^{3-6}/100 mL	Lake-river	U.S.	2
<0.3/L-5000/mL	Estuary (water column)	U.S.	19
460/g	Estuary (sediment)	U.S.	19
9.1%[b]	Raw well water	Canada	21
24%[b]	Drinking well water	Canada	21
9.6%[b]	Lake[c]	Canada	21
13%[b]	Lake[d]	Canada	21
6.6%[b]	River[c]	Canada	21
10%[b]	River[d]	Canada	21
8.8%[b]	Mixed source[c]	Canada	21
9.2%[b]	Mixed source[d]	Canada	21
8.8%[b]	New water main[c]	Canada	21
17%[b]	New water main[d]	Canada	21

Table 5. (Continued)

Organism concentration	Environment	Location	Ref.
36%[b]	Pre-reservoir[e]	Australia	27
95%[b]	Reservoir	Australia	27
79%[b]	Water distribution system	Australia	27
24%[b]	Underground water	Australia	25
98%[b]	Surface water	Australia	25
38%[b]	Reservoir[f]	Australia	25
96%[b]	Reservoir[g]	Australia	25
24%[b]	Reservoir[h]	Australia	25
94%[b]	Reservoir[i]	Australia	25
100%[b]	Water distribution system	Australia	25

[a] Mean concentration of extensive survey of waters throughout the U.S. Consult reference for extensive tables of concentrations.

[b] Percent of samples found to harbor Aeromonas spp.

[c] Raw water.

[d] Drinking water.

[e] Pre-treatment.

[f] From underground-water sources.

[g] From surface-water sources.

[h] Post-chlorination from underground-water source.

[i] Post-chlorination from surface-water source.

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CHAPTER 3. BACTERIA: The *Leptospira interrogans* Complex

ETIOLOGY AND CLINICAL DISEASE

The genus *Leptospira*, which is in the order Spirochaetales, family Treponemaceae, was formerly divided into *L. biflexa* and *L. icterohaemorrhagiae*. *L. biflexa* is a saprophytic, nonpathogenic species common in soil, water, and aquatic animals.[1,2] *L. icterohaemorrhagiae* is a parasitic bacteria that is the causative agent of leptospirosis, a disease of both medical and veterinary importance. Similarities such as survival and concentration in the environment that may exist between the saprophytic and parasitic leptospires are not clear.[1] This is probably the reason why *L. biflexa* and *L. icterohaemorrhagiae* are now contained in the species *Leptospira interrogans*.

There are over 170 serovars (formerly called serotypes; serovars are subdivisions of species or subspecies that are distinguished from one another on the basis of antigenic character) of *L. interrogans*. These serovars are divided into about 20 groups (e.g., serogroups) based on similarities between antigenic properties.[3] The most common serovars of *L. interrogans* in the United States are *pomona*, *autumnalis*, *icterohaemorrhagiae*, *hebdomadis*, *australis*, and *canicola*.[3,4] Commonly, the species of *Leptospira* is omitted (e.g., *interrogans*) and the serovars are used in identifying the organism of interest (e.g., *L. pomona*).

Leptospirosis was first recognized as a distinct clinical entity by A. Weil in 1886.[5] Severe cases with jaundice caused by *L. icterohaemorrhagiae* are still referred to as Weil's disease. The clinical picture of leptospirosis frequently is nonspecific,[6] and ranges from a mild or subclinical flu-like illness to a severe and rapidly fatal illness.[7,8] Ninety percent or more of all cases of leptospirosis are anicteric (i.e., not related to jaundice), and symptoms are those of an acute, self-limiting illness resembling many viral, rickettsial, and bacterial infections.[9] Common symptoms are fever, chills, headache, severe malaise, muscular aches, vomiting, and conjunctivitis. Less often there is meningeal irritation, jaundice, renal insufficiency, hemolytic anemia, skin and mucous-membrane hemorrhage,[3] and acute respiratory distress or failure.[6] Up to 10% of cases may suffer permanent partial disability and secondary manifestations, mainly involving the eyes.[10] The average duration of symptoms is 7.9 d, with a range of 3 to 22 d.[11]

Severity of leptospirosis is dependent on serovar, some of which are more virulent than others. Mortality also varies with serovar and other factors. One study in Brazil showed the mortality in four outbreaks to range from 3.3 to 24%.[12] Fatality in 133 other Brazilian cases was 7.5%.[13] A study conducted in Puerto Rico showed 6% mortality in overall cases and 13% mortality in icteric cases.[12] An outbreak in six trout-farm workers had a 16.7% mortality rate.[7]

Leptospirosis is the most widespread zoonosis (i.e., infection that is present in man and animals) in the world.[10] All the strains that can infect animals are potentially pathogenic to humans.[2] The disease results in abortion or stillbirth in pigs; jaundice, hemoglobinuria, and variable death rates in cattle and sheep; and sometimes abortion in cattle. Furthermore, death is not uncommon in young animals.[14]

Diagnosis of leptospirosis is confirmed by an increase in serological titers, by isolation of leptospires from blood during acute illness or from urine after the first week of the disease. Isolation requires special media or inoculation of experimental animals. The isolate can be confirmed with ELISA (enzyme-linked immunosorbent assay) or immunofluorescence techniques.[3]

Treatment is controversial: it is considered by many to be useless if started more than 3 or 4 d after the onset of symptoms. Not much evidence exists that antibiotics alter the course or outcome of the disease in humans.[15] Drugs used in treatment include high doses of streptomycin, penicillin, tetracycline, and erythromycin given early in the acute stage of the disease.[3]

Animals can be vaccinated to prevent disease but not necessarily infection. Human immunization against occupational exposure has been carried out in Spain, Italy, and Japan.[3]

OCCURRENCE

Leptospirosis has a worldwide distribution.[13] Reservoirs of infection and of one or more serovars have been found worldwide except for the polar regions.[3] Certain serotypes, such as icterohaemorrhagiae, pomona, and canicola are widespread, but others are found only in a few areas.[13] Multiple serotypes are found in most tropical areas.[16] The only cases reported in Asia were in Southeast Asia, Sri Lanka, and Japan.[3] Cases have been reported in Israel but not in other middle-eastern countries.[3]

Leptospirosis is both an occupational and recreational hazard for those who may come in contact with infected animals or their urine. Occupations that may be at risk include farmers, particularly in the Third World; field workers,[10] especially those working flooded fields; veterinarians; sewer workers;[4,16] miners; abattoir (i.e., slaughterhouse) workers; fish-farm workers; conservation workers;[17] and military troops.[3] Recreationally, bathers,[4,11] campers, fishermen, and hunters are potentially at risk.[3]

Leptospirosis is found more often in men than in women, probably because of exposure rather than true sexual predisposition.[16,18] The disease is found mainly in men of working age, from 15 to 64 y old.[4,5,13,18,19] Although it is more frequent in young adults, it is more lethal in older persons.[13] Outbreaks caused by swimming in contaminated water frequently involve young teenagers.[8,11] In an outbreak in Washington State associated with swimming in contaminated water, 86.9% of those affected were teen-age males.[11] The incidence in Papua New Guinea, shows no preference between men and women, who both have close contact with potentially infected animals.[16]

In temperate climates, leptospirosis frequently has a seasonal distribution, most cases being clustered in the summer and fall. Ninety-four percent of cases in Britain are evident between June and November.[18] In Thailand, incidence is highest in the period between the end of the rainy season and early winter (October through November).[20] Outbreaks may occur in swimming areas after dry periods, where water flow is limited,[4,11] particularly in July through November in the U.S.[4,5] Increased temperature appears to increase the number of cases.[21] In tropical areas, such as regions of Brazil, increased incidence in times of heavy rainfall has been reported.[13] Presumably, such incidence results from frequent contact with standing waters.

Leptospirosis cases can take the form of either sporadic cases or epidemic outbreaks.[12] Table 1 shows attack rates (e.g., rate of new cases per 1000 people exposed) expressed in terms of number of seroconversions (e.g., positive test for presence of antigen) for outbreaks in people in various regions throughout the world.

RESERVOIR

A large number of vertebrate animals, both wild and domesticated, can be the reservoir for leptospires. It is possible that all vertebrates are susceptible to the organism. Many or all Leptospira serovars have preferred hosts in which they are commensals, colonizing the kidney tubules without apparent harm to the animal.[16] Other animals can also be infected, and they may transmit the disease with or without symptoms[16] or evidence of seroconversion.[25] Rats and other rodents are the usual carrier hosts. Some animals, particularly rodents, may be carriers for life.[2,13]

Table 1. Attack rates for various serovars of Leptospira interrogans expressed in terms of number of seroconversions.

Area	No. seropositive per 1000 exposed	Description	Ref.
England	667	Outbreak, trout farm	7
U.S., U.K.	10	General population	19
Missouri	52	Veterinarians	17
Missouri	26	General population	17
Missouri	160	Conservation Commission	17
Washington	112	Swim outbreak, boys	11
Washington	67	Swim outbreak, girls	11
Washington	101	Swim outbreak, total	11
Tennessee	90	Swim outbreak	9
Argentina	66	Buenos Aires population	12
Argentina	187	Abattoir workers	12
Bolivia	49	Santa Cruz	12
Brazil	30	Sao Paulo, abattoir	12
Brazil	137	Hospitalized	12
Brazil	57	All types of workers	12
Columbia	20	Abattoir workers	12
Peru	27	Lima, market	12
Surinam	279	Jungle area	12
Guatemala	34	Agricultural workers	12
Haiti	33	Not reported	12
Jamaica	129	General population	12
Jamaica	329	Sugarcane workers	12
Mexico	182	Wide area	12
Panama	236	Ranch population	12
NE Cuba	699	Jaundice and fever victims	12
Havana, Cuba	100	Jaundice and fever victims	12
Haiti	301	Jaundice and fever victims	12
Jamaica	509	Undiagnosed fever	12
Trinidad and Tobago	93	Undiagnosed fever	12
Puerto Rico	139	General population	12
Lat. Am. Carib.	30-180	General population	12
Lat. Am. Carib.	20-320	Professional groups	12

Table 1. (Continued)

Area	No. seropositive per 1000 exposed	Description	Ref.
Lat. Am. Carib.	10-500	Undiagnosed fever patients	12
Brazil	150	Leptospirosis symptoms	13
N Thailand	4	General population	22
N and NE Thailand	2.7	General population	20
Bangkok	79.5	Hospitalized persons	20
Thailand	113	Provincial hospital	20
Thailand	96	Rural and urban hospitals	20
Indonesia	0.59	All febrile hospitalized patients	23
Malaysia	60	Febrile hospitalized patients	19
Malaysia	120	General population	19
Sumatra	230	Jaundiced, epidemic	24
Sumatra	46	Not jaundiced, epidemic	24
Sumatra	25	Control area	24
Israel	37	Outbreak, farmers at risk	10

Sources of the disease include cattle[15] and swine, which together cause more human infections in the U.S. than do rats.[17] Other potential reservoirs include sheep, goats, horses, dogs,[26] rats, mice, voles, shrews, hedgehogs, and other wild animals such as tortoises, frogs, waterfowl, bats,[27] foxes, skunks, deer, squirrels, raccoons, opossums,[28] sea lions,[3] bears, antelope, hares, and seals.[4,25,29] Dogs, rats, cattle, and swine are the most common carriers in cases where the disease source can be traced.[5]

MODE OF TRANSMISSION

Leptospirosis is transmitted through contact with water, moist soil, vegetation, or other materials contaminated with the urine of infected animals. It can also be transmitted by direct contact with urine or tissues of infected animals. Contact is usually through the skin, especially if abraded, or through the mucous membranes.[2-4,16] Body immersion in raw water, intentional or accidental, is frequently the mode of transmission.[2,8,9,11] Human-to-human transmission is rare.[13]

Of 130 attributable cases investigated in a 1959 U.S. study, 36% were linked to cattle or swine; 26% to swimming, drinking, or immersion; 16% to dogs; 13% to rats; 3% to wild animals; and 6% to other sources.[4] Another study performed in the U.S. could only attribute 1 in 4 cases to infecting sources; 31% of these were linked to rats; 30% to dogs; 21% to cattle; and 24% to swine.[5] A Brazilian study found the most frequent sources of infection for 133 cases were, in order of frequency: contact with sewage, 16.5%; rats, 15.8%; water, 11.3%; dogs, 5.3%; mud, 2.2%; and garbage, 1.5%.[13]

ENVIRONMENTAL PERSISTENCE

Under optimal conditions some Leptospira interrogans serovars are known to survive for significant periods of time. For a summary of survival studies, see Table 2.

Leptospira serovars survive longer in neutral-to-alkaline pH.[4,8,11,21] Okazaki and Ringen showed in 1957 that a pH below 6 or above 8.4 rapidly killed the organisms.[30]

Leptospires require moisture for survival. The (nonpathogenic) L. biflexa complex requires a moisture content of 65 to 71% as the minimum moisture allowing optimum growth.[1] Leptospires prefer moist soil, stagnant ponds, or slow-moving streams,[4] and they will not survive long in badly polluted water. Smith and Turner reported that the presence of Mycobacterium rubra and Escherichia coli permitted prolonged survival, whereas Pseudomonas spp. and Aerobacter cloacae prevented survival beyond 1 to 2 d.[31]

Leptospires apparently prefer temperatures greater than 22°C for infectivity.[4] The minimum growth temperature is 10 to 13°C.[1]

Animals can carry leptospires for significant periods. Cattle may shed them from weeks to several months, and leptospires have been found at distances 940 to 1000 m downstream from infected cattle sources.[11,21] Cattle, sheep, goats, pigs, horses, foxes, and dogs can carry leptospires for 120 to 700 d.[34] Rats can carry leptospires for life.[3]

DOSE RESPONSE

The infective dose has not been determined for humans. Studies in guinea pigs using L. icterohaemorrhagiae have displayed a lethal dose as low as one organism.[16,8] Studies using hamsters have determined a median infective dose of 4.7 organisms per hamster, with a range of 1 to 9 organisms per hamster.[35] The median infective dose for guinea pigs (subcutaneous) for L. icterohaemorrhagiae is reported to be 5.7 per animal, and and for L. autumnalis the guinea pig median effective dose is reported to be 6.8 organisms per animal.[8]

Table 2. Survival of Leptospira in the environment.

Conditions	Time[a]	Ref.
L. pomona:		
Salinity, 0.5–3.5%, 4–37°C	<24 h	16
Sea water	18–20 h	16
Water-saturated soil	183–193	30,31
Damp soil	3–5	30,31
Dry soil	2.5 h	30,31
River water, not sterile, pH 8	8	31
River water, sterile, pH 7.8	99	31
Rain water, not sterile, pH 7	12–18	31
Rain water, sterile, pH 7	21–42	31
Soil 1:10 in rain water	7–14	31
L. icterohaemorrhagiae:		
Buffered distilled water, pH 5.3	12–13	31
Buffered distilled water, pH 6.5	11–13	31
Buffered distilled water, pH 8	36–107	31
Buffered distilled water, pH 7.2	21–23	31
In environment	7–21	21
Manure, in oxidation ditch	61	8
Natural water, lab conditions	>13	8
River water, 5–6°C	8–9	16
River water, 20–27°C	5–6	16
River water, 31–32°C	3–4	16
Tap water + 10% sewage, 5–6°C	6–7	16
Tap water + 10% sewage, 25–27°C	3–4	16
Tap water + 10% sewage, 31–32°C	2–3	16
Tap water, room temperature	18–20	16
Tap water + bacterial flora	10–12	16
Undiluted sewage	12–14 h	16
Aerated sewage	2–3	16
Salinity, 30–40 mg/L	10	31
Salinity, 13,000–17,000 mg/L	<1	31

Table 2. (Continued)

Conditions	Time[a]	Ref.
L. australis:		
Soil, pH 6.1-6.2	43	31
Surface water, pH 6.6-7.6	24	31
River water, 27°C, pH 7	5-6	32
Soil with rat's urine, pH 6.7	8-15	32
Unspecified serovar:		
Feces	<24 h	16
Liquid cattle feces	5	16
Distilled water, 45°C	30 min	16
Distilled water, 50°C	10 min	16
Distilled water, 60°C	10 s	16
Distilled water, 70°C	<10 s	16
Soil	5	33
Dry meadow, 9.5-16.5% moisture	6-12 h	33
Reeds, willows, 70-77% moisture	14-15	33
Sedges, 41-65% moisture	3-7	33
Sterile tap water, pH neutral	28	16
Sterile tap water, pH 5	<2	16
Urine	<24 h	16

[a] Time in days unless noted otherwise.

LATENCY

Symptoms of leptospirosis generally develop after 2 to 19 d, with 7 to 10 d being the average.[16]

DISINFECTION

Studies reported in 1948 revealed leptospires to be more sensitive to chlorine than the enteric bacteria. The organisms are also highly susceptible to cationic, but not anionic, detergents.[16]

Leptospires survived aerobic digestion processes for up to 2 months, but remain viable less than 5 d in sludge or effluent from these processes. From this information, it is apparent that processes with aeration and short retention times, such as activated sludge and trickling filters, may not eliminate leptospires from effluent. Anaerobic processes such as septic tanks and processes retaining sewage for a week or more should destroy leptospires, generally within 30 h.[16]

Leptospires are heat-sensitive and will be destroyed by treatment processes using heat.[16] Refer to Table 2 for thermal death points of leptospires in distilled water.

MONITORING METHODS

Detection of pathogenic leptospires in the environment is difficult because of competing growth from other organisms and the trouble of differentiating pathogenic from saprophytic strains. The failure to isolate pathogenic leptospires from the environment does not necessarily indicate their absence. For example, qualitative methods are used to detect leptospires in the environment because the above problems and the organism's slow growth preclude quantitative determinations.

Samples of gently agitated bottom sediments in stream or pond water are filtered through a series of filters of decreasing coarseness. After the water has been cleared by gross filtering, leptospires can be separated from other bacteria by filtration through 0.45-μm pore filters. Leptospires can pass through these filters, whereas other bacteria generally cannot.[36]

Leptospira isolates are grown on Fletcher's semisolid enrichment media plus 10% rabbit serum at 30°C for up to 6 wk, and are examined by dark-field microscopy weekly for growth and/or contamination.[36]

After growth is established, the leptospires must be differentiated from saprophytic strains, which can grow at much lower temperatures (13°C on Stuart's medium with 10% rabbit serum) than the pathogenic species can grow. Other growth characteristics are also described in the Leptospira section of Standard Methods for the Examination of Water and Wastewater.[36] More than one test must be used for differentiation. Commercial antisera may be used to tentatively identify pathogenic leptospires. Final verification is made by intraperitoneal injection of the isolate into guinea pigs. The animals are sacrificed after 4 wk, and blood is tested for serum antibody-titer levels above 100 units. Leptospires should also be cultivated in Stuart's medium after being obtained from aseptically removed kidney tissue.[36]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

No indicator-organism/pathogen relationship exists for pathogenic Leptospira, and it is not likely that such a relationship will be developed because of the extreme variability of occurrence of pathogenic leptospires in the environment and the difficulty of isolation and enumeration.

ENVIRONMENTAL CONCENTRATION

Leptospires are frequently isolated from surface waters in areas occupied by infected cattle,[21] although this is not always the case.[9,11] The number of leptospires excreted in urine by animals or humans can amount to several tens or hundreds for a single microscopic field of vision.[34] Severely infected cattle were found to have up to 10^8 organisms per mL of urine.[21] Table 3 displays the proportion of animals in various areas globally that were found to either contain leptospires or to test positive serologically for the organism.

Table 3. Prevalence of leptospires in animals.

Area	Seropositive (%)	Description	Ref.
USSR	15	Frogs, Greek tortoises	27
USSR	13.2	Aquatic birds	27
New Zealand	34[a]	Black rats	37
New Zealand	26[a]	Brown rats	37
Australia	32.7	Cattle, outbreak	29
U.S.	10-50	Rodents	5
Tennessee	0.5-0.1[a]	Cows, upstream of outbreak	9
Idaho	8	Mule deer	29
Louisiana	55	Striped skunk	29
Quebec province	6.4	Cattle, *L. pomona*	29
Quebec province	17.8	Swine, *L. pomona*	29
Quebec province	10.3	Horses, *L. pomona*	29
Quebec province	0-6.7	Dogs and cats	29
Belgium	30	Horses	29
England	60	Cows, outbreak	15
SW England	23	Cattle	15
Israel	5.9[a]	Rats, scene of outbreak	10
Israel	33[a]	Mice, scene of outbreak	10
Israel	2.3[a]	Cattle, scene of outbreak	10
Israel	26.3[a]	Dogs, scene of outbreak	10
Orissa, India	18-50	Sheep, goats	29
Argentina	55	Cattle	12
Bolivia	71	Cattle	12
Brazil	23.6	Cattle	12
Colombia	14.7	Cattle	12
Chile	59-69	Cattle	12
Ecuador	12	Cattle	12
Peru	10	Cattle	12
Uruguay	39	Cattle	12
Mexico	22-39	Cattle	12
Guatemala	21-42	Cattle	12
Nicaragua	44	Cattle	12

Table 3. (Continued)

Area	Seropositive (%)	Description	Ref.
Panama	37-49	Cattle	12
Barbados	52	Cattle	12
Dominican Republic	85.7	Cattle	12
Guyana	49	Cattle	12
Jamaica	25	Cattle	12
Puerto Rico	32	Cattle	12
Trinidad and Tobago	35	Cattle	12
Argentina	50-65	Swine	12
Barbados	29	Swine	12
Brazil	7-20	Swine	12
Colombia	17	Swine	12
Guatemala	28	Swine	12
Guyana	16	Swine	12
Jamaica	29	Swine	12
Mexico	12-51	Swine	12
Peru	20	Swine	12
Trinidad and Tobago	38	Swine	12
Uruguay	39	Swine	12
Argentina	51	Horses	12
Bolivia	75	Horses	12
Colombia	30	Horses	12
Guatemala	5	Horses	12
Jamaica	33	Horses	12
Mexico	29	Horses	12
Uruguay	51	Horses	12
Barbados	1.5	Dogs	26
N. Nigeria	4.5[a]	Brown rats	25
N. Nigeria	6.8[a]	Cow kidneys	25
S. Sumatra	6.7	Rats	24

[a] These percentages are isolations, not seropositivity.

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CHAPTER 4. BACTERIA: Pseudomonas spp.

ETIOLOGY AND CLINICAL DISEASE

The Pseudomonas genus is a large group of Gram-negative, spore-forming, motile rods. Several members of the genus are capable of causing disease in humans. The more important of these organisms include Pseudomonas aeruginosa, P. fluorescens, P. maltophilia, P. cepacia, P. pseudomallei, and P. mallei.[1] Members of the genus that cause disease less commonly are P. putida, P. pseudoalcaligenes, P. putrefaciens, P. stutzeri, P. acidovorans, P. Alcaligenes, P. diminuta, and P. testosteroni.[1,2] Many other organisms in this genus are saprophytic and may contaminate human clinical specimens.[2] Table 1 lists potentially pathogenic pseudomonads and the diseases they can cause.

Pseudomonas aeruginosa is by far the most important of the Pseudomonas pathogens, most of which rarely infect the uncompromised host. Pseudomonas aeruginosa is the etiologic agent in outbreaks of hot-tub folliculitis, also called hot-tub or whirlpool dermatitis, and Pseudomonas folliculitis.[6] This organism is also the agent in the majority of cases of otitis externa (inflammation of external auditory canal).[21]

In hot-tub folliculitis, the main symptom is a rash covering much of those parts of the body that directly contact the contaminated water, excluding palms of hands, soles of feet, and mucous membranes. Generally, the head and neck are spared.[6] The rash may be most severe in areas covered by bathing suits.[22] Associated symptoms, affecting up to one half of the cases, include weakness, muscle pain, chills, headache, fever, earache, swollen axillary lymph nodes, sore throat, and tender breasts.[6,21,23] The rash has been known to last as long as 21 d,[21,24] with an average of 7 to 10 d.[25] However, recurrences have been known to occur.[21] There is no indication that antibiotic treatment is necessary or useful,[21] and few cases are treated.

Otitis externa has also been linked to Pseudomonas aeruginosa through a wealth of circumstantial evidence.[9-11,26,27] Symptoms are that of a typical earache.

Most of the other pseudomonads are of limited virulence and invasiveness, but can produce extensive lesions under favorable circumstances.[2]

Most hot-tub folliculitis outbreaks have been associated with P. aeruginosa serovar 0-11.[24,28-31] Serovars 0-1, 0-6, and 0-9 have also been reported in such outbreaks.[29,32] Serovars 0-1 and 0-11 have been implicated in otitis externa outbreaks as well.[10,33]

Table 1. Diseases caused by Pseudomonas species.

Pathogenic organism	Disease	Ref.
P. aeruginosa	Opportunistic infections in patients with metabolic, hematolic, and malignant diseases; nosocomial infections from catheters, tracheostomies, etc.; infections in immunosuppressed and immunocompromised patients; surgical wounds; burns; traumatic wounds; lungs.	1
	Meningitis	3–5
	Blue-nail syndrome, swimmer's ear, toe-web infections, secondary infections of chronic ulcers, skin wounds, burns.	6
	Corneal ulcers	7
	Ecthyma granulosum	8
	Otitis externa	9–11
	Septicemia in hospitalized leukemic patients (up to 50% incidence)	5
P. fluorescens	Rarely pathogenic, may contaminate blood and blood products	1
	Opportunistic infections	2
	Sepsis from transfusions	12
P. maltophilia	Opportunistic, nosocomial infections	1,2,13,14
	Pneumonia	15
	Meningitis, primary	16
P. cepacia	Isolated from humans; plant pathogen	1
	Opportunistic infections	2
P. pseudomallei	Melioidosis, a zoonosis	1,17
P. mallei	Glanders, a zoonosis (horses)	1,6
P. stutzeri	Isolated from humans, saprophytic?	1
	Opportunistic infections	2
P. multivorans	Wound infections of varying severity	18
P. terrigena	Primary bacteremia, acute bacterial endocarditi (also called Comamonas terrigena)	15
P. putida	Opportunistic, nosocomial infections	2
	Sepsis from blood transfusions	12

Table 1. (Continued)

Pathogenic organism	Disease	Ref.
P. pseudoalcaligenes	Opportunistic, nosocomial infections	2
P. putrefaciens	Opportunistic infections	2
P. paucimobilis	Nosocomial infections	19
P. thomasii	Nosocomial infections	20

Hot-tub folliculitis is generally not treated. It is self-limiting and is not considered to be life-threatening.

OCCURRENCE

Pseudomonas aeruginosa has a worldwide distribution. Pseudomonas pseudomallei appears mainly to affect humans and animals in Southeast Asia, although a few cases have been reported in South and Central America and the Middle East.[1,17,34] The distribution of the other pseudomonads has not been determined.

Pseudomonads appear to have both an exogenous habitat, (i.e., free living in soil, water, and plants), and an endogenous habitat, (in the human body).[2] Pseudomonas aeruginosa is known to multiply outside the host in warm, moist environments[35] and can grow relatively quickly in distilled water.[36] It is almost a universal inhabitant of wet areas such as sinks and baths, and is probably autochthonous (native) to natural waters.[37] Pseudomonas maltophilia is found widespread in nature, and is frequently isolated from water and raw milk.[15]

Pseudomonas pseudomallei is a soil organism and is frequently isolated from soil, clay, and muddy water in Southeast Asia, Iran, and Australia.[17] It appears to have a higher disease prevalence during the wet season in Australia, which is February to May.[17]

Hot-tub folliculitis appears to strike young people, ages 10 to 19, more frequently; however, this is usually attributed to increased exposure in this age group.[22,26] When all ages are exposed, attack rates are similar regardless of age or sex.[11,24] In temperate climates, the incidence of infection of both hot-tub folliculitis and otitis externa increases in the warm summer months.[3,11]

Table 2 lists attack rates (i.e., rates of new cases) of hot-tub folliculitis and otitis externa in reported outbreaks.

RESERVOIR

In humans, the large intestine is the in vivo reservoir for Pseudomonas aeruginosa, and about 3 to 11% of healthy persons harbor the bacteria.[39] Glanders (a chronic debilitating disease caused by P. mallei) is found on the skin or in the lungs of infected horses, and the reservoirs of melioidosis (caused by P. pseudomallei) are rats, mice, rabbits, dogs, and cats, all of which carry the bacteria in the intestine.[39] Pseudomonas aeruginosa generally is not harbored by animals except those in close contact with humans. Pseudomonas maltophilia is a common commensal or contaminant of clinical specimens and is part of the transient intestinal flora of hospitalized patients.[14] All of the pseudomonads are found free living in the environment, which is the major reservoir.

MODE OF TRANSMISSION

Hot-tub folliculitis and otitis externa are both transmitted through contact with contaminated water.[3,4,10,21,22,24,28,30-32,33,38,40-44] Frequent swimming can increase the risk of otitis externa.[9,11,44] Nosocomial (disorders associated with treatment in a hospital) and secondary infections with the pseudomonads may be transmitted through contaminated disinfectant, soak, wash, and rinse solutions used in hospitals,[7,13,18,19] trauma or surgery,[6] blood transfusions,[12] dialysis,[45] and contaminated hydrotherapy tanks.[35] Urinary tract infections may result from catheterization.[36,39]

Some reported infections from unusual pseudomonads have been of unknown origin.[15,16] Others are more well-defined; for instance, glanders is transmitted by skin contact or inhalation of bacteria from infected horses.[39] Melioidosis is transmitted through infected arthropod vectors, water, or food.[39]

SUSCEPTIBILITY AND RESISTANCE

Because not all persons exposed to P. aeruginosa-contaminated water and nosocomial Pseudomonas infections become ill, some host factors must play a role in determining immunity to the pseudomonads. However, the pattern of immunity is not understood.[21] Many pseudomonad infections occur as secondary and nosocomial infections and are not found in normal, healthy people.[6]

Table 2. Attack rates of outbreaks involving Pseudomonas aeruginosa.

Location	Attack rate/1000	Description	No. exposed	Ref.
Toronto, Canada	167	OE,[a] pool	24	11
Aberdeen, U.K.	720	OE, pool	-	10
New Zealand	875	HTF,[b] spa pool (I)[c]	8	29
Utah	760	OE, HTF (I)	152	26
Minnesota	857	HTF, whirlpool (I)	49	4
Minnesota	530	HTF, pool and spa (I)	61	22,31
Atlanta, GA	850	HTF, whirlpool	-	38
Atlanta, GA	530	HTF, whirlpool	-	38
Tennessee	620	HTF, pool (I)	-	24
Pennsylvania	600	Wound infections (I)	-	35
Connecticut	800	HTF, whirlpool	10	25
North Carolina	83	HTF, hot tub (I)	24	33
North Carolina	167	OE, hot tub (I)	24	33
Vermont	800	HTF, whirlpool (I)	-	32
Wyoming	428	HTF, pool and sauna carpet	-	30
Napa, CA	1000	HTF, hot tub	6	21
Napa, CA	833	HTF, hot tub, this outbreak	-	3
?	902	HTF, hot tub, exposed	41	28
?	118	HTF, hot tub, controls	34	28

[a] OE = otitis externa.

[b] HTF = hot-tub folliculitis.

[c] (I) = evidence of inadequate disinfection present.

Current research is involved in developing a vaccine against P. aeruginosa. Such a vaccine would be used for burn patients, those with slow-healing wounds, the immunocompromised, and other at-risk groups. Preliminary reports of the vaccine's effect in rabbits and mice are promising; no trials in humans have yet been attempted.[46,47]

ENVIRONMENTAL PERSISTENCE

Although Pseudomonas aeruginosa is essentially an aquatic organism and does not tolerate desiccation well,[37] it has better survival characteristics than do coliforms.[48] Table 3 shows the resistance of various Pseudomonas species to drying and storage under experimental conditions.

P. aeruginosa can be a tenacious contaminant of hot-water lines, and attempts to decontaminate the lines have been unsuccessful.[19,20] Pseudomonas aeruginosa has been frequently reported to thrive in pools and spas with acceptable disinfectant residuals.[51,52] (The Disinfection section contains information on resistance to chlorine.) Some authors have concluded that Pseudomonas cannot be eliminated from the walls of public spas merely by maintenance of an appropriate free-chlorine level of $\geq$1 mg/L and a pH of 7.2 to 8.0; the spa sides must also be scrubbed, and/or the water must be replaced.[53] In one study, showering with soap was reported to afford some protection from hot-tub folliculitis.[40] In other studies, however, no such protection was reported.[11,22,31]

Pseudomonas aeruginosa is reported to survive longer in human feces than in animal feces, although the exact time is not specified.[54] The bacteria can infect plants, insects, and animals,[6] and algal blooms are reported to stimulate its growth.[37]

In some studies, no clear association has been noted between pH and Pseudomonas aeruginosa persistence in chlorinated waters. Table 4 reports isolations of P. aeruginosa at various pH levels found in public spas. These data, however, should be used with caution; the chlorine residuals corresponding to the various pH readings are not given. Also, the data are based on percent isolation, and therefore give no quantitative measure of the magnitude of reduction.

DOSE RESPONSE

The median infective dose for P. aeruginosa or the other Pseudomonas species is not known.[24,28,56]

It has been reported that as little as 1 to 2 min of exposure can lead to hot-tub folliculitis,[24] but 15 min is a minimal time more often quoted for infection.[25,32] In one study, 5 of 7 exposed persons became ill following a 15-min exposure.[25] In this same outbreak, all of the 3 persons exposed for 30 min became ill. Quantitative bacterial counts of the water were not made.[25] The total duration of exposure to a contaminated hot tub over a 4-d period was associated with illness in another study. In that study,

Table 3. Survival of Pseudomonas under drying and/or storage conditions.

Organism	Time (d)	Description	Ref.
P. aeruginosa	7-14	SDTW[a], dried	49
P. aeruginosa	>30	SDTW, air-dried, 0% humidity	49
P. aeruginosa	>7	Storage, dried, 40°C	49
P. aeruginosa	1	Storage, dried, 60°C	49
P. aeruginosa	<1	Storage, dried, 80°C	49
P. aeruginosa	3	Rapid drying	49
P. aeruginosa	<1	Dried on glass squares	50
P. aeruginosa	3	Stationary phase, desiccated	50
P. cepacia	<1	SDTW, dried	49
P. cepacia	3	Air-dried, 0% humidity, SDTW	49
P. fluorescens	>30	SDTW, dried	49
P. fluorescens	>30	Air-dried, 0% humidity, SDTW	49
P. fluorescens	>7	Storage, dried, 40°C	49
P. fluorescens	<1	Storage, dried, 60°C	49
P. fluorescens	<1	Storage, dried, 80°C	49
P. maltophilia	>30	SDTW, dried	49
P. maltophilia	>30	Air-dried, 0% humidity, SDTW	49
P. maltophilia	>14	Rapid drying	49

[a] SDTW, dried = sterile, dechlorinated tap water mixed with the Pseudomonas sample and dried.

patients had a mean duration of exposure of 10.2 h, whereas nonpatients averaged 5.1 h exposure.[33] Studies of other outbreaks have not found significant correlations between duration of exposure and illness.[24]

In otitis externa, a direct correlation was found between length of exposure to water and type of bacterial flora resident in the ear canal. Otitis externa occurred in all experimental cases where water exposure predisposed the host to such changes in microbial flora (e.g., in divers). In these cases, P. aeruginosa was the organism most often associated with otitis externa.[9]

Table 4. Effect of pH on Pseudomonas aeruginosa isolations in public spas and swimming pools.

pH	No. spas tested	Positive isolations[a] (%)	Ref.
Public spas:			
<6.8	3	33	51
6.8-7	5	40	51
7.1-7.3	8	37	51
7.4-7.6	11	55	51
7.7-7.9	10	20	51
≥8	13	23	51
Swimming pools:[b]			
6.8-7		22	55
7.1-7.3		0	55
7.4-7.6		16	55
7.7-7.9		12	55
≥8		7	55

[a] Here, a positive isolation is a successful attempt to isolate P. aeruginosa from a medium. For example, as shown in the first line of the table, three spas were tested, and 33% of the samples were positive for P. aeruginosa.

[b] A total of 100 pools were tested.

LATENCY

In the literature, the latency period for hot-tub folliculitis from P. aeruginosa ranges from 8 h to 7 d.[6,22,24,26] The average latency is about 2 to 2.5 d.[24-26,40,42]

DISINFECTION

A large amount of information is available on the effect of disinfectants on Pseudomonas aeruginosa. The Centers for Disease Control guideline for swimming pools is to maintain a free-chlorine residual of more than 1.0 mg/L and to regularly hyperchlorinate public spas and hot tubs.[21] However, P. aeruginosa is found frequently to persist in pools despite proper chlorination.[24,52] A spa from which P. aeruginosa was isolated in one study had a free-chlorine residual of 20 mg/L.[51] This high residual was accompanied by a high pH, which decreases chlorination efficiency. In other studies, chlorine levels of 2 to 3 mg/L were reported to be ineffective when the pH was above 8.0.[24] Chlorine effectiveness may be adversely affected by higher temperature and by organic debris from heavy usage.[21] Cleaning, in addition to disinfection, appears to be necessary.[53]

Table 5 summarizes percent of isolation of P. aeruginosa from pools and whirlpools with varying disinfectant residuals. It must be noted that percent positive isolations is by no means a quantitative measure, and conclusions from these data must be drawn carefully.

In the disinfection of therapeutic Hubbard tanks and hospital waterbeds, 200 ppm total-available chlorine was found to be effective in disinfection.[35,59] The Centers for Disease Control recommend sodium hypochlorite at a free residual of 15 ppm in the tanks when in use.[35]

In one reported outbreak of dermatitis from a hot tub, regrowth of P. aeruginosa after disinfection was examined. The once-daily chlorine dose was 35 mg/L. At time zero, there was no detectable P. aeruginosa. At 0.2 h, the level was 10^6 organisms/100 mL, and at 22 h, there were 2.8×10^5 organisms/100 mL.[28] These researchers did not specify if Pseudomonas originated from bathers or areas of the hot tub that were relatively protected from disinfection. Also, the researchers did not measure chlorine residuals at the times of Pseudomonas enumeration.

An examination of public spas and hot tubs in San Diego, CA, found an average free-chlorine level of 6.4 mg/L in hot tubs free of P. aeruginosa, and an average of 3.8 mg/L in spas in which the organism was isolated.[53] Excessive slime or biofilm production may increase chlorine resistance of some P. aeruginosa strains.[54,60]

Chlorine at 0.2 mg/L residual was found to eliminate 85 to 94% of P. aeruginosa after 1 min at a pH of 7.4 under laboratory conditions. Twice that amount (0.4 mg/L) killed 92 to 99.7% of the organisms.[54] It was found that 1 h is required for 0.5 mg/L residual chlorine at pH 7.2 to kill 99.9% of P. aeruginosa organisms in natural waters; in swimming pools with a high bather load, this same chlorine amount would require 1 to 3 h to kill 99.9% of the organisms.[61]

An iodine concentration of 3 ppm was found to kill 85% of the bacteria in 2 min, and 97% in 18 min.[35] Studies of iodine as a swimming-pool disinfectant reveal that P. aeruginosa is not eliminated completely by iodination used in acceptable amounts in pools.[62]

Table 5. Isolation of Pseudomonas aeruginosa from pools disinfected with chlorine.

Free-chlorine residual (mg/L)	Positive isolations (%)	Description	Ref.
0	42	100 pools, Australia	55
0.1–0.9	24	100 pools, Australia	55
1–1.9	0	100 pools, Australia	55
2–2.9	0	100 pools, Australia	55
3–3.9	0	100 pools, Australia	55
≥ 4	0	100 pools, Australia	55
≥ 0.3	1.8	Pools, Florida	57
TC ≥0.3[a]	10.2	Pools, Florida	57
TC <0.3[a]	27.3	Pools, Florida	57
0	43.7	Pools, Florida	57
<0.10	58	Netherlands, free chlorine	3
0.10–0.29	30	Netherlands, free chlorine	3
≥ 0.30	0	Netherlands, free chlorine	3
0.0–0.9	62	Public spas	51
1.0–1.9	29	Public spas	51
2.0–2.9	43	Public spas	51
3.0–3.9	0	Public spas	51
≥ 4	11	Public spas	51
≤ 0.7	93.7	16 pools, Colorado	58
0.2	Outbreak[b]	Whirlpool, pH 7.8	24
0.3	Outbreak[b]	Whirlpool, pH 7.6	24
0	Outbreak[b]	Pool, pH 7.2	24
0.5	Outbreak[b]	Pool, pH 7.2	24
0.3	Outbreak[b]	Whirlpool, pH 7.5	24
0	Outbreak[b]	Pool, pH 8	24
0	Outbreak[b]	Whirlpool, pH 7.2	24
0	Outbreak[b]	Whirlpool	24

[a] TC = total chlorine.

[b] These figures were taken from reports of hot-tub folliculitis or otitis externa outbreaks.

A study using bromine as a disinfectant in a whirlpool spa concluded that 10 mg/L residual bromine was effective in controlling P. aeruginosa levels with bathers present.[60]

The pseudomonads are characterized by their ability to use a wide range of carbon sources, thus explaining their ability to thrive and grow in medicinal solutions such as procaine and benzalkonium chloride. Instruments stored in such solutions can become heavily contaminated.[39] P. multivorans is reported to grow in a 1:30 solution of Savlon in amounts up to 10^9 organisms per 100 mL.[13,18] Savlon is a disinfectant solution of chlorhexidine hydrochloride at 0.05% and centrimide at 0.5%.

In general, Pseudomonas aeruginosa may not be decreased by biological oxidation processes during wastewater treatment. In 69% of cases in one study, multiplication occurred in aerobic processes in the laboratory and in trickling filters.[63] Multiplication up to 30 times the original number can occur.[27] There is confusion in the literature on this point, however, as other researchers report a decrease of P. aeruginosa by as much as 99% in secondary sewage treatment.[27]

MONITORING METHODS

Section 914 of Standard Methods for the Examination of Water and Wastewater, 16th edition,[64] contains two (tentative) methods for isolation of P. aeruginosa. The first is a membrane-filter technique that involves filtering less than 200-mL portions of natural water or up to 500 mL of swimming-pool water through sterile membrane filters. The filters are laid on M-PA agar plates and incubated at 41.5°C for 72 h. The colonies typically have light edges with brownish to greenish-black centers. Milk agar is used as confirmatory media. P. aeruginosa hydrolyzes the casein in this media and produces a yellow-green diffusible pigment.[64]

The second method uses a multiple-tube technique in which five 10-mL, five 1-mL, and five 0.1-mL samples of the water to be tested are put into asparagine broth. Higher dilutions may be necessary for natural waters. The tubes are incubated at 35 to 37°C and examined under a UV light in a darkroom at 24 and 48 h. Production of a greenish fluorescent pigment completes the presumptive test. The confirmed test is the production of purple color, indicative of high pH, on acetamide agar slants or broth inoculated from positive presumptive tubes. These tubes are incubated at 35 to 37°C and examined at 24 and 36 h.[64]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

Pseudomonas aeruginosa has been suggested as an indicator organism for the presence of pathogens in recreational waters of various kinds.[48] However, for the most part, it is too variable to be reliable as an indicator.[48] Although P. aeruginosa cannot be used alone, it may be useful in the form of a Pseudomonas-to-fecal coliform ratio as a measure of the proximity of pollution. Pseudomonas aeruginosa survives longer in the environment than do fecal coliforms, and ratios less than 2.5 are associated with immediate sources of fecal pollution.[48]

The presence of P. aeruginosa in surface water generally indicates human contamination.[27] However, there is no correlation between P. aeruginosa and Escherichia coli, a commonly used indicator organism for the presence of pathogens in drinking waters[27] or swimming-pool waters.[55]

Coliform bacteria were absent in 117 of 227 drinking-water specimens that were found to be positive for P. aeruginosa in a Hungarian study.[65] Even where total coliforms were detected, P. aeruginosa outnumbered them. In the same study, no coliforms were found in 70 to 80% of specimens from industrial-water-cooling circuits that were identified as positive for P. aeruginosa.[65]

One study that examined the indicator potential of P. aeruginosa found a significant difference in numbers of indicators isolated at varying times of day for all organisms tested except P. aeruginosa.[66] This may suggest that P. aeruginosa is not as sensitive to fluctuations in pollution as other possible indicators, adding to the case against its use as an indicator of fecal contamination.

ENVIRONMENTAL CONCENTRATION

Sewage is probably the major source of Pseudomonas aeruginosa in surface waters.[24] Organisms reported to infect distilled water or other aqueous hospital solutions include P. aeruginosa, P. maltophilia, P. putida, P. flucrescens, P. thomasii, and P. paucimobilis.[7,12,13,16,19,20] Pseudomonas multivorans was found in concentrations of up to 10^7 organisms/mL in a Savlon disinfectant solution in a hospital outbreak of this organism.[18] Table 6 summarizes the recorded concentrations of P. aeruginosa from various environmental samples.

Table 6. Concentration of Pseudomonas aeruginosa in the environment.

Location	Concentration (% or per 100 mL)[a]	Description	Ref.
Cleveland, OH	50–83	Water, Edgewater Beach	66
Mentor, OH	3–12	Water, Headlands Beach	66
Hot tub	100,000	Outbreak[b]	28
San Diego, CA	2400	Public spa, maximum recorded	51
San Diego, CA	195	Public spas, average	51
U.S.	200–490	Storm drainage outfall	27
U.S.	1–10	Surface waters	27
U.S.	100–1000	Polluted streams	27
U.S.	0.5–13%	Healthy ears	27
U.S.	65.5–80%	Ears, otitis cases	27
U.S.	11%	Healthy adults, gut	27
Madison, WI	225,000	Sewage, average, y	27
U.S.	10^5–10^6	Estimate, sewage	27
Wyoming	2.8 x 10^9/g	Carpeting, outbreak	30
U.S.	77.6%	Swimmers, otitis	44
U.S.	33.3%	Nonswimmers, otitis	44
U.S.	10.5%	Swimmers, controls	44
U.S.	4.3%	Nonswimmers, controls	44
Atlanta, GA	33	Median, 3 pools	38
Mississippi River	<1.4	Wisconsin to Minnesota	37
Mississippi River	33.8%	Water samples	37
Mississippi River	46.4%	Fish	37
Mississippi River	67.7%	Sediment	37
Mississippi River	46.8%	Plants	37
Mississippi River	63.3%	Aufwuchs (i.e., botanical organism)	37
U.S.	10^5/cm^3	On skin = infection	8
U.S.	5 x 10^5/cm^3	Average infected density	8
Florida	400–10^5	Natural recreation waters	67
Germany	26–49 x 10^5	Wastewater, activated sludge	63
Hungary	3.4–22.3%	Drinking water	65
Hungary	37.2%	Chlorinated municipal water	65
Hungary	23.4–84.4%	Mineral water	65

Table 6. (Continued)

Location	Concentration (% or per 100 ml)[a]	Description	Ref.
Hungary	66.2%	Well water	65
Hungary	95.7%	Industrial water circuits	65
Hungary	3.4%	Swimming pools	65
Hungary	22.3%	Surface waters	65
Hungary	16.5%	Sewage	65
Germany	33,000	Sewage	27
New Zealand	10^9	Surface, spa pool	29
New Zealand	8×10^8	Subsurface, spa pool	29
Netherlands	≤ 350	Whirlpools, outbreaks	3

[a] Numbers with % are percentages of positive isolations found.

[b] Outbreak figures are those measured after reported outbreaks of otitis externa or hot-tub folliculitis.

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CHAPTER 5. BACTERIA: Staphylococcus spp.

ETIOLOGY AND CLINICAL DISEASE

The genus Staphylococcus is made up of Gram-positive, spherical cells (cocci) that grow in a characteristic grape-like pattern. These cocci are responsible for a wide variety of infections and disease syndromes.[1,2] The "type" pathogen in the genus is Staphylococcus aureus, although S. epidermides has also been isolated frequently from superficial infections. Although staphylococcal infections may not be a direct result of water contact, poor water quality or lack of water (i.e., personal hygiene) may lead to opportunistic staphylococcal infections. "The most common cause of derangement is a break in the skin surface; other causes include insect bites, parasitic infestations, dermatologic disease, and conditions in the host that effect immunologic status or granulocyte function."[3]

Table 1 contains a list and definitions of soft-tissue infections related to S. aureus.[3-5] Staphylococcal bacteremia can result in 80% mortality if untreated.[6] Severe sinusitis can result in death from sinus thrombosis and bacterial meningitis.[7]

Skin is a natural inhibitor of many pathogens because of its physical and chemical nature. Lipids inhibit Gram-positive cocci, whereas surface dryness inhibits Gram-negative organisms.[3] It is also thought that sweat possesses some antibiotic components.[3]

Many toxins are associated with Staphylococcus, six enterotoxins, alpha and beta endotoxins, and exfoliation toxin, to name a few.[8,9] Skin abrasions, furuncles, or other localized infections may serve as a source for exfoliative toxin.[8] Exfoliative toxin produces a disease known as "Scalded Skin Syndrome" (SSS), in which the toxin-producing organism "...causes cleavage of the middle layers of the epidermis, bulla formation, and ultimately, slippage of the superficial layer of the epithelium on gentle pressure...".[8] Healing can be rapid with treatment by localized care and antibiotics (i.e., beta-lactam, cephalosporins, erythromycin, vancomycin).[8] However, the past indiscriminate use of antibiotics has resulted in the development of many antibiotic-resistant strains of pathogenic Staphylococcus.[10] Therefore, initial isolation must be accompanied by antibiotic-resistance tests.[10]

A schematic diagram (Fig. 1) illustrates the passage and migration of S. aureus and Streptococcus.[11]

Table 1. Staphylococcus spp. soft-tissue infections.

Infection	Description
Superficial	
Impetigo	Inflammatory skin disease, characterized by the appearance of pustules. Also known as pyoderma.
Ecthyma	A pustular eruption, usually seated on a hardened base and encircled by an inflammatory base.
Deep (localized)	
Folliculitis	Inflammation of a follicle or follicles.
Furuncle (boil)	A painful nodule formed in the skin by circumscribed inflammation of the corium and subcutaneous tissue, enclosing a central slough ("core").
Carbuncle	A necrotizing infection of skin and subcutaneous tissue, with multiple formed or incipient drainage sinuses and an indurated border around the lesion.
Abscesses	Localized collection of pus in a cavity formed by the disintegration of tissues.
Staphylococcus SSS[a]	Caused by the production of exfoliative toxin by the Staphylococcus organism. The result is cleavage of the middle layers of epidermis with sloughing of the epidermis under mild pressure.
Deep (nonlocalized)	
Cellulitis	Inflammation of cellular tissue, especially purulent inflammation of the loose subcutaneous tissue.
Erysipelas	Contagious, infectious disease of the skin and subcutaneous tissue marked by redness and swelling of affected areas, and with constitutional symptoms.

[a] Scaled Skin Syndrome (SSS).

Prevalence of infection sites in Brazilian natives has been identified, in decreasing order, as arms/hands, legs/feet, and ears.[12] In volunteers from a developed country, prevalency was found to be, in decreasing order, legs/thighs, backs, and arms.[13] These differences were thought to be due to skin thickness and/or blood flow, and the occurrence of lesions.[12,13]

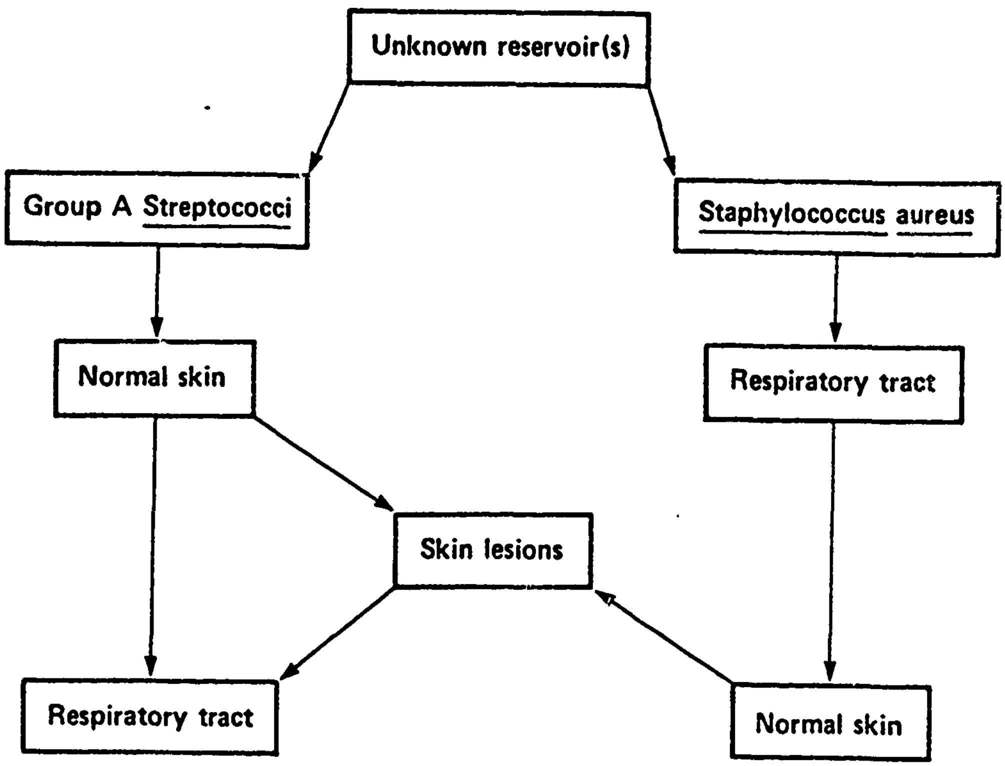

Figure 1. Passage and migration of Staphylococcus aureus and Streptococcus. From Dejani et al.[11]

OCCURRENCE

Staphylococcus spp. are ubiquitous, and are especially a problem in areas of poor sanitation under crowded conditions and/or where water supplies are limited in quantity and/or quality. For example, a survey of four Brazilian villages revealed that pyoderma occurred in 11% of the population.[12] It has been estimated that 20 to 30% of all persons are chronic carriers, whereas 70 to 90% are transient carriers. Reasons for this estimate are unclear.

RESERVOIR

Humans are the primary reservoir for staphylococcal disease.[2]

MODE OF TRANSMISSION

Mode of transmission is primarily by person-to-person contact, with one third of infections caused by autoinfection.[2] Persons with draining lesions or any purulent discharge are the most common source of epidemic spread.[2] It has been shown that contact with water is beneficial for pathogenic flora on the epidermis;[14] therefore, the spread of staphylococcal disease may occur via the water route.

SUSCEPTIBILITY AND RESISTANCE

Immune mechanisms are not well understood; however, patients with Staphylococcus SSS develop antibodies against the exfoliative toxin.[15] This apparently confers immunity against future exposures. Some individuals are more susceptible than others, particularly newborns, the elderly, and the immunocompromised.[2]

ENVIRONMENTAL PERSISTENCE

Staphylococcus spp. are found in waters frequented by humans,[14,16-19] with the highest numbers occurring in swimming pools and bathing areas. The survivability of Staphylococcus spp. in swimming pools is dependent upon the type and concentration of disinfectant, the contact time, and the pH of the water (see Disinfection section). In sewage, Staphylococcus has been isolated from 95% of water samples collected in a developing country.[20] In natural waters, Staphylococcus spp. may survive for long periods; however, certain green algae secrete strong antibiotic compounds that can lead to a 20 to 30% decline per day in bacteria (including Staphylococcus).[21]

DOSE RESPONSE

The dose-response information obtained from the literature search is presented in Table 2. As shown in Table 2, the dose range is extremely broad. As might be expected, the effective dose depends on several factors: trauma, local skin environment, health of patient, and mode of entry.[11,24,25] In a review of 123 patients suffering from staphylococcal infections, Musher and McKenzie[26] reported that 78% had soft-tissue infections (STI) due to breaks in skin. Of this group, 23% suffered from bacteremia. Deep STI occurred in 75% of the patients observed; many of these began as infections of hair follicles.

Although most of the doses shown in Table 2 correspond to high concentrations that typically will not be found in the environment, it should be noted that Staphylococcus, under optimum conditions, has a generation time of 0.5 h, and under such conditions it would take a single cell less than half a day (i.e., 12 h) to produce a population of 10^6 cells.[24]

LATENCY

The time it takes for Staphylococcus spp. to become established in hair follicles or traumatized areas of the skin is less than 24 h. These data were presented in Table 2. Dajani et al.[11] have estimated that it would take 11 d for an infection of Staphylococcus located in the main reservoir in humans (the nares) to migrate to the normal skin and to develop into skin lesions resulting in impetigo. Therefore, the time it takes Staphylococcus to establish an infection is dependent upon the severity of the wound, dose of Staphylococcus, and location of the wound.

DISINFECTANTS

Most research has focused on disinfectants for Staphylococcus that are either applied topically or are used in swimming pools. Table 3 contains some of these data.

The topical antiseptics hexachlorophene ("pHisohex") and chlorhexidine are useful primarily for cleaning skin and lesions of Staphylococcus.[3] Generally, the agens that are used for disinfection of swimming pools, such as chlorine, bromine, and iodine, are

Table 2. Staphylococcus dose response on humans.

Dose	Response (%)[a]	Latency (d)	Ref.
200 to 500[b]	Not specified	–	22
0.3 to 0.6[c]	100		23
2×10^6 to 8.5×10^6 [d]	100 (19/19)	<1	24
10^2 to 10^5 [d]	0 (0/26)		24
5×10^6 [e]	0 (0/2)		24
7×10^4 [f]	0 (0/4)		24
10^8 to 10^9 [g]	0 (0/5)		24
3×10^4 [h]	100 (2/2)		24
300 [h]	100 (1/1)		24
$>10^6$ [i]	100		24
8.7×10^6 to 7×10^9 [j]	6 (2/35)[k] 13 (10/78)[ℓ]	≥1	13 13
2×10^2 to 2×10^6 [m]	100[n]		25

[a] $\text{Percentage} = 100 \times \frac{\text{no. positive infections}}{\text{total no. tested}}$.

[b] Minimal colonizing dose on infants (expressed as number of organisms).

[c] Exfoliative toxin (expressed as μg of toxin).

[d] Intradermal application (expressed as number of organisms).

[e] Subcutaneous application (expressed as number of organisms).

[f] Skin incision (expressed as number of organisms).

[g] Topical application, no lesions (expressed as number of organisms).

[h] Organisms coated on suture (toxic shock syndrome may have also been present) (expressed as number of organisms).

[i] Range with trauma, overall (expressed as number of organisms).

[j] Applied to skin on agar cups (range, expressed as number of organisms).

[k] With trauma.

[ℓ] Without trauma.

[m] Range of organisms (expressed as number of organisms).

[n] Intradermal application, not reproducible.

Table 3. Effect of disinfectants on Staphylococcus.

Disinfectant	Dose	Response[a]	Time (min)	Ref.
Hexachlorophene[b]	-	Reduces colonization	-	22
(pHisohex)	-	Inhibits Gram (+) organisms	-	3
Chlorhexidine[b]	-	Inhibits Gram (+) and Gram (-) organisms	-	3
Bromine	< 2 ppm	Regrowth of organisms	-	27
	> 2 ppm	100	-	27
Chlorine	1 ppm	100	240	3
Combined chlorine	1.0 mg/L[c]	99.99 (pH 6.0)	5	19
	1.0 mg/L[c]	99.98 (pH 7.0)	5	19
	1.0 mg/L[c]	76.00 (pH 9.5)	5	19
	1.0 mg/L[d]	99.7 (pH 6.0)	5	19
	1.0 mg/L[d]	98.5 (pH 7.5)	5	19
	1.0 mg/L[d]	58.0 (pH 9.5)	5	19
Iodine	0.35 mg/L[c]	99.0 (pH 7.5)	0.5	19
	0.35 mg/L[d]	99.0 (pH 7.5)	0.66	19
Chlorine	0.35 mg/L[c]	99.0 (pH 7.5)	0.33	19
	0.35 mg/L[d]	99.0 (pH 7.5)	0.5	19
Chlorine	0.03 ppm	100	95	28
Ultraviolet	-	99	-	29
30% Hydrogen peroxide	90 mg[e]	100	15-30	30
	90 mg[f]	>99.99	60	30
	90 mg[g]	>99.99	180	30
CaOCl	2.5 ppm[h]	100	1-2	31
	1.0 ppm[h]	100	2-3	31
	10 ppm[i]	100	2-5	31
	5 ppm[i]	100	>240	31

Table 3. (Continued)

Disinfectant	Dose	Response[a]	Time (min)	Ref.
Organic chloramine[j]	2.5 ppm[h]	100	30-60	31
	1.0 ppm[h]	100	>60	31
	10 ppm[i]	100	>120-240	31
	5 ppm[i]	100	>120-240	31

[a] Unless otherwise stated, numbers represent % removal.

[b] Topical disinfectant.

[c] Staphylococcus aureus.

[d] Staphylococcus epidermidis.

[e] 10^2 S. aureus.

[f] 10^{3-5} S. aureus.

[g] 10^6 S. aureus.

[h] Clean water (22.5°C).

[i] High organic load (4°C).

[j] 3-Chloro-4,4-dimethyl-2-oxazolidinone.

only effective under optimum conditions. These conditions include pH values of 6 to 7, with temperatures at 22 to 25°C, and with good water quality, as measured in terms of nephelometric turbidity units (i.e., <1 NTU).[19,31] Most of the data in Table 3 was generated from in vitro experiments with water of good quality. Williams et al.[31] have shown that there can be dramatic differences in time to achieve 100% kill in waters with high organic loading (Table 3).

In chlorinated swimming pools, Staphylococcus have been shown to survive 4 to 10 h with chlorine concentrations greater than 1.0 ppm.[17] Hydrogen peroxide is considered a good initial sterilizer; however, Yoshpe-Purer and Eylan[30] have shown that the addition of low levels of chlorine are necessary to maintain a protective residual.

MONITORING METHODS

Two procedures are recommended by Standard Methods for the Examination of Water and Wastewater, 16th ed., for the identification and/or quantitation of Staphylococcus spp.[32] The first procedure, as outlined in Section 914A (i.e., modified multiple-tube procedure to obtain a most-probable number (MPN) index), describes a method for isolating and enumerating Staphylococcus spp. from swimming-pool water. If the water source contains chlorine, sodium thiosulfate (100 mg/L) must be added to sampling jars to neutralize the chlorine. The second procedure is the Presence-Absence (P-A) Coliform Test (Section 908 E) with the isolation of Staphylococcus on mannitol salt agar.

Membrane filtration techniques were previously included in Standard Methods, but they have since been found to be too inconsistent[18] and have been excluded from the most recent edition.[32]

Media, such as Vogel-Johnson or Baird-Parker agars, are being developed to isolate and differentiate between Staphylococcus spp.[16] Also, rapid-identification kits are available commercially; however, these will work only on pure cultures.[4]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

Staphylococcus is an indicator of skin-pathogen presence, because it is a potential skin pathogen itself.[28,32] Staphylococcus can survive in chlorinated waters better than coliforms: therefore, the use of coliforms does not provide any information about the Staphylococcus content in these waters.[17,19,28] There is only a small amount of information comparing Staphylococcus concentrations to concentrations of typical "indicators" such as coliforms, mainly because Staphylococcus is representative of a different source of pathogen contamination (i.e., oral-nasal instead of fecal). Crone and Tee, in a 5-y study of monitoring swimming pools, found that of the Staphylococcus spp. isolated, 65% were pathogenic S. aureus.[17] Another study has suggested that 100 Staphylococcus organisms per 100 mL represents potential for infection,[28] whereas others have suggested that zero Staphylococcus organisms per 100 mL[17] be used as standards for bathing waters. One study of the bacterial content in the city drains of a developing country (Nigeria) found that S. aureus was recovered from 95% of all samples that were coliform-positive.[20]

ENVIRONMENTAL CONCENTRATION

Only a small amount of information was recovered by this literature search on the concentration of Staphylococcus spp. in the environment (excluding swimming pools). As previously mentioned, one study found that S. aureus was recovered from 95% of all samples from a drainage system in a city of a developing country (Nigeria).[20] The concentration of staphylococci is apparently dependent upon the use of the water source by infected or naturally shedding humans.

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CHAPTER 6. BACTERIA: Non-cholerae Vibrio spp.

ETIOLOGY AND CLINICAL DISEASE

The genus Vibrio is comprised of short, slightly curved, Gram-negative, rod-shaped bacteria that inhabit brackish-to-saline environments. Recently, several newly recognized species of Vibrio have been associated with diseases other than gastroenteritis in humans.[1] More and more, species other than V. cholerae (i.e., V. vulnificus, V. parahaemolyticus, and V. alginolyticus) have been associated with wound infections and sepsis.[1] In either case, common symptoms include fever, chills, nausea, vomiting and, occasionally, death. Of the three listed above, V. vulnificus presents the most severe infections, causing edema, ulcers, and deep necrosis in soft tissue.[1,2]

The previously described pathology is associated with the recently determined surface virulence component of the V. vulnificus bacterium. This surface virulence was found to be part of the lipid-polysaccharide portion of the cell wall.[3] Vibrio vulnificus also produces a V. cholerae-like hemolysin that can be used as a virulence marker.[4] Once established in a local infection site, V. vulnificus develops a fulminating infection, resulting in site and nonsite skin ulcers as well as general sepsis with major organ involvement.[2] It has been reported that up to 41% of patients with septicemia have died suffering from hypotension and hemochromatosis.[2]

Vibrio parahaemolyticus is recognized primarily as a cause of diarrhea via food poisoning, but it is frequently isolated from wound infections and infrequently associated with septicemia[2] and pneumonia.[5] Vibrio alginolyticus infections also result in the formation of ulcers[2]; however, our literature search revealed no information to indicate the occurrence of septicemia as a result of V. alginolyticus infection.

Treatment of V. vulnificus can range from use of antibiotics (tetracycline) to surgery, as stated by Blake, "Thirty-eight percent of the patients with primary septicemia underwent surgical procedures.." which included, "...debridement, incision and drainage, fasciotomy and leg amputation...".[2] Treatment of V. alginolyticus and V. parahaemolyticus generally consists of antibiotic treatment with occasional surgical treatment of infected wounds.

OCCURRENCE

Infections that do not involve the gastrointestinal tract, but are produced by non-cholerae Vibrio spp. have been reported in North America, Europe, Asia, and

Australia.[2] Most of these reports are from the U.S. and this is probably due to special interests of American researchers. In a 1981-1982 survey of reported Vibrio spp. infections, 30 cases were the result of infection by V. vulnificus.[1] As stated above, Vibrio parahaemolyticus, long considered to be restricted to gastrointestinal diseases, has since been isolated frequently from wound infections incurred in salt or brackish waters. Vibrio alginolyticus was unrecognized as a human pathogen until 1973, and then within a 3-y period, almost 50 cases had been cited in the literature.[2]

Tackett et al.[1] examined the relative risk of developing sepsis or wound infections in exposed individuals (Table 1). As shown in Table 1, the relative risk of individuals acquiring a vibrio related infection in a wound following exposure to saltwater or shellfish is 11 times greater than for individuals not exposed. The relative risk of an individual developing primary sepsis is 15 times greater if the individual ingests raw oysters or suffers from any chronic diseases. Most infections due to Vibrio spp. occur during the warmer months of the year.[2]

RESERVOIR

The reservoirs for non-cholerae Vibrio spp. are estuarine and salt-water environments.[2]

MODE OF TRANSMISSION

Vibrio spp. infect by direct contact of open wounds by marine waters or sediments, or, in the case of V. parahaemolyticus, by the ingestion of seafood containing these organisms.[1,2]

SUSCEPTIBILITY AND RESISTANCE

Susceptibility to Vibrio spp. is generally universal to those persons at risk (see Table 1). The previously described surface virulency component[3] enables the V. vulnificus organism to evade in vivo phagocytosis and complement-mediated lysis. However, preliminary studies that have used this component as an immunizing agent have shown that protection is possible.[3] Further studies along this line of research are being conducted.

Table 1. Relative risk[a] of developing sepsis or wound infections by individuals exposed to Vibrio vulnificus.

Type of exposure or medical history of exposed individual	Relative factor[a]
Primary sepsis	
Raw-oyster ingestion	15
History of liver disease	8
Use of antacids or cimetidine	1
History of diabetes mellitus	5
History of malignancy	1
Any chronic disease	15
Wound infections	
Exposure to salt water or shellfish	11
History of malignancy	5
History of liver disease	3
History of diabetes mellitus	2
Any chronic disease	7

[a] Relative risk can be expressed quantitatively as a risk factor, which is equal to the incidence of disease in an exposed group divided by the incidence of disease in an unexposed group.

ENVIRONMENTAL PERSISTENCE

Information is limited relative to the survival of non-cholerae Vibrio spp. in the environment. It is known that Vibrio spp. are indigenous to warm, marine environments. This fact was demonstrated in a study by Tilton and Ryan,[6] who found that V. alginolyticus could be isolated from seawater samples at temperatures of 18 to 22°C. The minimum growth temperature for this organism is 8°C.[2] Vibrio vulnificus was not isolated until seawater temperatures were at least 21°C. Once the seawater had warmed up (August), the following order (decreasing) was found for most commonly isolated vibrios: V. alginolyticus, V. vulnificus, V. parahaemolyticus, and V. fluvialis.

Fujioka and Greco have also isolated Vibrio spp. from brackish water (16 ppt) and freshwater ponds (1 ppt) used for aquaculture.[7] In general, non-cholerae Vibrio spp. do not grow under conditions of low NaCl concentration.[8]

Recently, Watkins and Cabelli[9] reported that V. parahaemolyticus densities are increased indirectly when fecal pollutants are introduced into an estuary. This indirect relationship is based on the increase in copepods, which supply a chitinous surface that V. parahaemolyticus uses as a nutrient source.

DOSE RESPONSE

Our review of the literature did not identify any information concerning the dose of non-cholerae Vibrio spp. necessary to cause wound infections or sepsis in humans.

LATENCY

Our review of the literature did not identify any information concerning the latency of non-cholerae Vibrio spp. that cause wound infections or sepsis in humans.

DISINFECTANTS

Our review of the literature did not identify any information concerning the effects of disinfectants on non-cholerae Vibrio spp. However, the effect of disinfectants on V. cholerae is presented in a previous report (Volume 5 of this series).[10] It might be assumed that the effect of disinfectants on non-cholerae Vibrio spp. could be similar, but further work in this area is necessary.

MONITORING METHODS

In environmental samples, Vibrio spp. are found primarily in seawater and estuarine environments. The concentration techniques for Vibrio spp. are similar to those described for Salmonella in Standard Methods for the Examination of Water and Wastewater, 16th ed. (Sec. 912 A.1.); however, a sample size of 1 to 10 L is suggested.[11]

Enrichment for Vibrio spp. is described in Standard Methods, 16th ed. (Sec. 912 G.2).[11] For example, to inhibit the growth of competitive, antagonistic organisms, an alkaline (pH 9.0) peptone water medium is suggested. To achieve selective growth for primary isolation, thiosulfate-citrate-bile salt-sucrose agar (TCBS agar) is the medium of choice. Vibrio vulnificus and V. parahaemolyticus appear blue-green, whereas V. alginolyticus appears yellow on this medium. Most of these methods for the recovery of Vibrio spp. are qualitative and not quantitative. Biochemical tests are required to identify bacterial colonies from this agar. These methods are outlined in Standard Methods, 16th ed. (Sec. 912 G.4),[11] and in clinical microbiological manuals.[8] Also, serological identification is possible with slide agglutination or fluorescent antibody reagents prepared in the laboratory.

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

Standard indicator organisms do not reflect the presence of non-*cholerae* *Vibrio* spp. because (1) *Vibrio* spp. occur naturally in brackish and salt water and are not necessarily a result of human activity; and (2) coliforms (total or fecal) do not survive well in environments that the *Vibrio* spp. inhabit.[12] A study of indicator organisms performed off the coast of Denmark revealed that there was no correlation between *Vibrio* spp. and fecal and total coliforms.[12] As previously stated, *V. parahaemolyticus* was found to correlate with fecal pollution in an estuary.[9] However, it was thought that this resulted from increased populations of copepods, which *V. parahaemolyticus* feeds upon.[9]

ENVIRONMENTAL CONCENTRATION

Vibrio spp. are found throughout marine and brackish-water environments.[6,7,12] Environmental concentrations of *Vibrio* spp. identified by our literature review are presented in Table 2. In the past, *Vibrio cholerae* has attracted most of the attention for the genus *Vibrio*. A summary of the environmental concentrations of that organism is contained in Volume 5.[10] It has been only recently that concern for other *Vibrio* spp. has prompted interest in concentrations of these organisms in the environment. Also, the current methods for determining numerical concentrations of these non-*cholerae* *Vibrio* spp. have been somewhat limited.

Table 2. Environmental concentration of Vibrio spp.

Vibrio spp.	Concentration[a]	Environment	Location	Ref.
V. anguillarum	$\geq 10^3$/100 mL	Marine-brackish[b]	Denmark	12
V. alginolyticus	$\geq$ 500 /100 mL	Marine-brackish	Denmark	12
V. alginolyticus	$3 \times 10^{4-6}$ cfu/mL[c]	Marine	Long Island, NY	9
V. parahaemolyticus	1 to 500/100 mL	Estuary	Rhode Island	7
Vibrio spp.	1/mL	Marine well	Hawaii	6
Vibrio spp.	250 to 3000/mL	Brackish	Hawaii	6
Vibrio spp.	30 to 7000/mL	Freshwater ponds[d]	Hawaii	6
Vibrio spp.[e]	5×10^2 to 3×10^4 cfu/mL			6
		Marine	Long Island, NY	9

[a] Concentration given as number of organisms of Vibrio spp. isolated.

[b] Bathing beach, harbor, stream, disposal plant, sandy floor.

[c] cfu/mL = colony-forming unit/mL.

[d] Outdoor aquaculture pond with salinity of 1 ppt.

[e] Sucrose-negative vibrios (V. parahaemolyticus and V. vulnificus).

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CHAPTER 7. PROTOZOA: Acanthamoeba spp.

ETIOLOGY AND CLINICAL DISEASE

Acanthamoeba spp. are the causative agents of amebic meningoencephalitis (AM), an infectious disease that is essentially confined to the central nervous system (CNS).[1] Acanthamoeba spp. (i.e., A. culbertsoni, A. castellanii, A. polyphaga, and A. astronyxis) are free-living amebas found in water and soil.[1,2] This genus poses a threat to those individuals in contact with water or soil containing Acanthamoeba, but primarily it is a problem to the chronically ill or immunocompromised individual.[1-3] These organisms infect the human host via "...the respiratory tract, genitourinary system or skin, reaching the CNS by hematogenous spread."[1] Also, entry occurs from lesions of the skin.[2,4] Having gained entry to the human host, Acanthamoeba spp. seeks the brain, a secondary target. This infection involves "...the midbrain, basal areas of the temporal and occipital lobes and posterior fossa structure."[1]

Clinically, this disease is characterized by insidious onset and prolonged course.[2] Symptoms of AM include headache, nausea, vomiting, and stiff neck, progressing to coma and death.[1] Diagnosis of this disease is accomplished by the examination of fresh CNS fluid and direct observation of Acanthamoeba spp. trophozoites (vegetative stage of life cycle) and/or characteristic "wrinkled-wall" cysts.[1,4,5] Acanthamoeba polyphaga has been shown also to infect the cornea of the human eye; although it is generally not lethal.[6]

Sulfadiazine treatment for Acanthamoeba infections has been reported to be successful.[4,7]

OCCURRENCE

Amebic meningoencephalitis caused by Acanthamoeba spp. has been reported from many areas of the world, with the exception of Europe and the USSR.[2] However, Acanthamoeba spp. have been isolated from various freshwater and soil sources, including tap water and swimming pools worldwide.[6,8-10] Attack rates for this disease have not been documented.

RESERVOIR

Acanthamoeba spp. are free-living amebae found in soil and water.[2,11] There have also been several isolations from freshwater fish.[12,13]

MODE OF TRANSMISSION

As mentioned previously, Acanthamoeba spp. infect skin lesions, the respiratory tract, and the genitourinary system via contact with contaminated water or soil and reach the CNS by hematogenous spread from the point of exposure.[1,2]

SUSCEPTIBILITY AND RESISTANCE

Mechanisms of susceptibility and resistance to Acanthamoeba are unclear. This disease occurs most frequently in chronically ill and immunosuppressed individuals. However, it has been isolated from the lungs of healthy persons; therefore, most persons may be considered resistant.[1,2] The immune response typically involves phagocytic activity, along with the production of antibody. A protective immune mechanism to this parasite has not been identified.[14] Vaccine development using laboratory animals by Rowan-Kelly and Ferrante[15] has shown that protection in animals is possible. With a single inoculation of sonicated Acanthamoeba culbertsoni, 40% survival was achieved in the immunized animals; but with multiple immunizations, up to 80% survival was achieved.[15]

ENVIRONMENTAL PERSISTENCE

Under typical seasonal conditions, Acanthamoeba spp. can survive indefinitely in soil and fresh water. This genus has also been isolated from brackish and salt water.[5,16] These organisms can survive a wide range of temperatures, having been isolated from water sources at temperatures from 2 to 46°C.[9] The higher incidence of infection by free-living amebae from warmer waters most probably reflects the activities (i.e., swimming) of humans than that of the amebae.[9] However, it has been demonstrated that Acanthamoeba recovered from environments of warm (30 to 45°C) thermal outfalls (or thermal muds) possess much greater virulency than those isolated from cooler environments.[17] The optimum pH for Acanthamoeba is pH 7.0, and this organism has been shown to survive low concentrations of dissolved oxygen (2.8 to 3.1 mg/L).[16]

DOSE RESPONSE

No information was found in our literature search on the dose necessary to cause disease or infection in the human host. However, intranasal inoculation of 2.5×10^4 A. culbertsoni organisms into mice resulted in 100% death in the test animals.[15]

LATENCY

It is thought that the clinical symptoms for Acanthamoeba spp. infection are not displayed until more than 7 d after exposure.[1,2]

DISINFECTION

The effect of disinfectants on Acanthamoeba spp. is presented in Table 1. As indicated, this genus (both trophozoite and spore-form) is relatively resistant to the effect of chlorine and bromine, compared to other pathogenic protozoans (i.e., Naegleria).[16,18-20] A survey of swimming pools by De Jonckheere[21] has shown that Acanthamoeba spp. have been recovered from waters with chlorine residuals ranging from 0.0 to greater than 4.0 mg/L.

De Jonckheere and van de Voorde[20] have shown that trophozoites of Acanthamoeba spp. can survive up to 3 h with a chlorine residual concentration of 4.0 mg/L, and the cysts can survive up to 24 h with a residual chlorine concentration of 40 mg/L. Cursons et al.[19] compared the amebicidal properties of chlorine, chlorine dioxide, ozone, and Deciquam 222. Acanthamoeba was found to be the most resistant amebae to chlorine and chlorine dioxide; however, all amebae tested were equally sensitive to ozone and Deciquam 222. The type of disinfectant used under in situ conditions was found to be dependent upon the quality of the water.[19]

MONITORING METHODS

Currently no standard methods have been developed to monitor Acanthamoeba spp. in water.[22] However, it would be possible to use the same methods used for the isolation of Giardia and Entamoeba as described in Section 912 K of Standard Methods for the Examination of Water and Wastewater, 16th ed.[22] Examination and identification of Acanthamoeba from a concentrated sample can be accomplished by standard laboratory methods.[5]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

Our literature search identified only one study that correlated indicators to the presence of Acanthamoeba in drinking and bathing waters. This information is presented in Table 2. As shown, the presence of amebae does not correlate with sewage pollution.

Table 1. Effects of disinfectants on Acanthamoeba spp.

Disinfectant			Removal	
Chemical	Dose (mg/L)	Time	(%)	Ref.
Bromine	1.7-2		57[a]	18
Chlorine	0.1		40[a]	18
Chlorine	0.2-0.49		21[a]	18
Chlorine	0.2-0.49		28[a]	18
Chlorine	0.5-0.69		0[a]	18
Chlorine	0.5-0.89		40[a]	18
Chlorine	0.25[d]	30 d	100	19
Chlorine	4.0	180 d	(+)[a,b]	20
Chlorine	40.0	24 h	(+)[b,c]	20
ClO_2	2.9[d]	30 d	99.99[e]	19
ClO_2	2.5[d]	30 d	99.99[f]	19
Ozone	6.75[d]	30 d	99.9[e]	19
Ozone	6.75[d]	30 d	99.999[f]	19
Deciquam 222	0.025[d]	30 d	99.99[e]	19
Deciquam 222	0.025[d]	30 d	99.99[f]	19

[a] Acanthamoeba trophozoites.
[b] (+) = Acanthamoeba present at end of exposure to disinfectants.
[c] Acanthamoeba cysts present at end of exposure to disinfectant.
[d] Initial concentration.
[e] Acanthamoeba castellanii.
[f] Acanthamoeba culbertsoni.

Although Escherichia coli was used in the cultivation of Acanthamoeba in the laboratory, it is apparent that the presence of E. coli and other coliforms is not necessary for Acanthamoeba propagation in the environment.

Table 2. Indicator-organism/pathogen relationship for Acanthamoeba spp.[a]

Site	Samples positive for amebae and negative for coliforms (%)[a]	Samples positive for amebae and negative for Escherichia coli (%)
A	56	60
B	70	73
C	71	75

[a] Derived from Ref. 18.

ENVIRONMENTAL CONCENTRATION

Limited data describing the environmental concentrations of Acanthamoeba were found in our literature search. A survey of public swimming pools in France by Pernin and Riany[8] revealed that 25% contained Acanthamoeba. Another survey of drinking water and swimming pools in France and Belgium resulted in recovery of free-living amebae from 50 and 38% of samples, respectively. Acanthamoeba was found to be the dominant amebae isolated during this survey.[18,21] In Norway, 100% of frozen bathing waters were sampled and found to be positive for free-living amebae.[9]

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CHAPTER 8. PROTOZOA: Balantidium coli

ETIOLOGY AND CLINICAL DISEASE

Balantidium coli is a ciliated protozoan that can infect the human large intestine and cause the diarrheal disease, balantidiasis. Balantidium coli is the largest intestinal protozoan of humans, and both trophozoites (vegetative form) and resistant cysts can be found in infected individuals.[1,2]

Up to 80% of infections are asymptomatic, with the organism living as a commensal in the lumen of the colon.[3] In symptomatic cases, the clinical picture is diarrhea or dysentery, often chronic in nature.[4] There may be abdominal pain; tenesmus; and blood, mucus, and pus in the stool.[5] There may be 6 to 15 liquid stools per day in moderately acute infections.[1] Severe infections closely resemble amebic dysentery, with tissue invasion and marked ulceration, but metastatic spread is rare.[6,7] However, B. coli has been known to cause acute appendicitis, vaginitis, cystitis, peritonitis, intestinal perforation, and septicemia.[3,4,8] In fatal cases, multiple and diffuse ulceration and gangrene occur, and death may result from dehydration or blood loss.[1] In the tropics, mortality rates of 5 to 35% have been reported.[3]

It is believed that damage to the intestinal wall by other parasites such as Trichuris trichiura (whipworm, threadworm) may predispose patients to B. coli infection or invasion.[2,8]

Balantidiasis resembles many other dysenteries and enteric fevers. Diagnosis must be made by the identification of trophozoites or cysts in fresh feces.[1,3,9] Sometimes, diagnosis is made from identification of trophozoites obtained from material taken during sigmoidoscopy.[1,9]

Balantidiasis is treated with antibiotics; tetracycline, ampicillin, and diiodohydroxyquinoline are used commonly.[1,3] Metronidazole and paromomycin are also useful.[1,9]

OCCURRENCE

Balantidium coli has a worldwide distribution, but its incidence of infection is low.[2,9] Until 1960, only a few more than 700 cases were reported worldwide.[4] It is found most commonly in the tropics and subtropics, areas where sanitation is poor, and where pigs and humans are closely associated.[3] New Guinea and parts of South America appear to be the only places where infection is common, and it is generally asymptomatic in these areas.[7]

The highest prevalence of balantidiasis in areas where the disease is endemic is among teen-agers and adults.[3] In a waterborne outbreak on Truk in the Caroline Islands, distribution was equal between the sexes and among various age categories. Some reports state that females and children in Papua New Guinea have a higher infection rate, resulting from their closer association with swine; women may have twice the incidence of men in this area.[7] Other reports state that the disease is even more rare in children than in the general population.[10]

Table 1 displays information on the prevalence of B. coli infection in the few areas where it has been investigated.

RESERVOIR

The most common reservoir for B. coli is the pig,[7,8,11,12] and to a lesser extent the rat.[3,8] Prevalence in pigs is generally 50 to 100%.[3] Humans are also reservoirs.[9] Balantidium coli has also been reported in guinea pigs, cattle and other ruminants, dogs, cats, frogs, cockroaches, gorillas, a kangaroo, and a camel.[7,8,20]

Certain populations in New Guinea with endemic B. coli infections have unusually intimate contact with pigs. In areas where the nights are very cold, pigs are reported to commonly sleep with the women and children. Until the early 1960's, women were known to breastfeed piglets.[3,7]

MODE OF TRANSMISSION

Infection with B. coli occurs via the oral route. The main modes of transmission of B. coli infection appear to be contamination of food, water, utensils, and fingers by feces of pigs or humans infected with the protozoan. Direct fecal-oral contact can also transmit balantidiasis.[3]

Flies may also transmit the infective cysts or trophozoites.[9,10] Outbreaks generally are traced to water contaminated by swine feces.[9,11] Over 25% of human cases have shown some association with swine.[21]

SUSCEPTIBILITY AND RESISTANCE

Not much is known about the susceptibility of humans and other animals to balantidiasis.[4] It would appear that humans are naturally resistant to B. coli;[3,7,9] attempts to experimentally infect human volunteers have failed.[21] However, debilitated

Table 1. Prevalence of Balantidium coli infection.

Location	Attack rate[a]/1000	Description	Ref.
Caroline Islands	11.8	Moen village, Truk[b]	11
Truk district	3.7	Overall attack rate	11
Worldwide	0.7–7.7	Estimate	11
Venezuela[c]	40	Children, houses with water	12
Venezuela[c]	90	Children, houses without water	12
Venezuela	60	Total average	12
W. New Guinea	152	General population, 4 districts	13
W. New Guinea	70–280	Range, 4 districts	13
Nairobi	0.075	Hospital patients, 1944	10
Great Britain	0	3000 healthy persons, 1921	10
USSR	51	General population, 1943	10
Ethiopia	0–150	1923 Central Plateau villagers	14
Nigeria	1.3	6213 patients, Benin City	15
Amazon	60–100	Acculturating tribes	16
Amazon	0	Newly contacted tribes	16
Venezuela	10	Poor children	17
Venezuela	8	General population	18
Seychelles	13	Symptomatic, on Praslin	19
New Guinea	17	Highlands, all ages	7
New Guinea	110	West highlands, general population	7

[a] Attack rate is the rate of new cases of the disease.

[b] Truk Island balantidiasis outbreak. Moen village was the biggest focal point of the outbreak.

[c] Town of Pampanito.

persons or those individuals compromised by other diseases may be prone to more serious, even fatal, balantidiasis.[9] B. coli is an opportunist and is known to have heightened invasiveness when concomitant with other intestinal parasites.[2,8]

ENVIRONMENTAL PERSISTENCE

Only a small amount of information has been reported on the persistence of B. coli cysts or trophozoites in the environment. One study found trophozoites able to survive for 10 d at room temperature under anaerobic conditions.[6] From 10 to 80% of the trophozoites from many strains of porcine and human balantidia can survive when heated to 47°C for 20 min, and 50% of some strains can survive cooling to room temperature for 5 d in culture.[22] The cysts are reported to remain viable for weeks in moist feces.[10]

It is suggested that stool samples should be examined within 30 min to be sure that motile trophozoites can be identified; although, in rare instances, motile balantidia have persisted up to 6 h or longer in stool samples.[10] The trophozoites and cysts are killed rapidly by desiccation.[3]

No information is available on inactivation of B. coli by sewage treatment. It is assumed that cysts would respond like those of Entamoeba histolytica to sewage-treatment processes.[3]

DOSE RESPONSE

The median infective dose for B. coli is not known. Attempts to experimentally infect healthy human volunteers with 6 to 250 cysts or trophozoites were unsuccessful.[21] It is thought that the infective dose of B. coli may be similar to that of E. histolytica or Giardia lamblia, about 10 to 100 cysts.[3]

LATENCY

The incubation period for B. coli is not known, but it may be as short as a few days.[9]

DISINFECTION

No information is available on the disinfection of B. coli cysts or trophozoites. This is probably a result of its low incidence; consequently, balantidiasis is not considered to be a sufficiently significant public health problem to warrant disinfection studies.[3]

MONITORING METHODS

No monitoring methods for B. coli have been developed.

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

No indicator-organism/pathogen relationship has been found for B. coli.

ENVIRONMENTAL CONCENTRATION

No information is available on the concentration of *B. coli* in the environment. It is reported that far fewer *B. coli* cysts are produced per person in outbreaks of balantidiasis than *E. histolytica* cysts are produced in outbreaks of amebiasis.[3]

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CHAPTER 9. PROTOZOA: Naegleria spp.

ETIOLOGY AND CLINICAL DISEASE

The free-living ameba-flagellate Naegleria spp., an opportunistic pathogen, are responsible for the rapidly fatal human disease, primary amebic meningoencephalitis (PAM).[1-3] This organism can be recovered from the environment in one of three forms: cyst, ameba, or flagellate.[2] This limax (i.e., sluglike) ameba invades the human host via the nasal mucosa, penetrates the cribiform plate, and infects the subarachnoid space and brain.[1,2,4] Symptoms of PAM include headache, fever, lethargy, rhinitis, and pharyngitis. Nausea and vomiting are followed by meningeal irritation, and by the fourth or fifth day, the patient becomes comatose and disoriented. Also, by this time, convulsions occur, and finally death after about 6 d.[1,2,4] This disease usually affects healthy children or young adults with a recent history of swimming in freshwater pools or lakes.[1,2,4,5] Diagnosis is accomplished by the demonstration of the Naegleria organism in the cerebrospinal fluid of the patient.[2,6] Naegleria cysts, unlike Acanthamoeba, have never been observed in brain tissue.[2]

To date, antibiotic treatment has been successful on only two occasions.[2,7] The most common drug regime employed is amphotericin B in conjunction with rifampin and/or miconazole.[2] Tetracycline and rifampin with amphotericin B has been shown to be effective in mice.[2] However, it should be noted that amphotericin B may be extremely toxic to humans.[2,3]

OCCURRENCE

Primary amebic meningoencephalitis has been reported worldwide, and the Naegleria spp. have been isolated from swimming or thermal bathing pools,[8,9] spas,[10,11] thermal outfalls,[10,12-14] still-water lakes,[5] ponds,[15] and backwater bays.[10] Isolations from aquatic environments occur most frequently during summer months.[16] However, a survey of thermal outfalls in Belgium revealed that 55% of samples were positive for Naegleria during summer months and dropped to only 40% during the winter.[12]

Lawande et al. surveyed children in Zaire, Nigeria, and found that 27% had recoverable amebae from their nasal passages, 4% of which were pathogenic N. fowleri.[17] Because these children had not been swimming, it was assumed that dust was the vector. Surveys of large populations have shown that Naegleria spp. are recoverable from the nasal passages of healthy individuals. In one study, about 2% (38 people out of a population of 2289) of those examined were harboring the Naegleria organisms, whereas another survey of military recruits reported 5% of 1000 harbored Naegleria spp.[4]

RESERVOIR

This organism is free-living in the aquatic and soil habitats.[3] It has also been isolated from infected fish.[18]

MODE OF TRANSMISSION

Naegleria infection is acquired by contact with waters or dust containing the Naegleria organism.[3,17,19] Activities such as swimming, especially diving, in which water may be aspirated into the nasal cavity, may lead to introduction of Naegleria to the nasal mucosa.[3] There is an increased risk of disease associated with swimming in stagnant ponds, lakes, or thermal springs in warm climates during the summer months.

SUSCEPTIBILITY AND RESISTANCE

The characteristics of host susceptibility to PAM is not clear, because apparently normal individuals become infected.[3] As previously stated, up to 5% of a population may harbor the Naegleria organism; however, because actual disease occurrence is so low, one would assume a general resistance in most populations to the establishment of PAM. There is some evidence from studies with primates to support the presence of resistance, but this seems to depend on the route of exposure (i.e., no clinically detectable signs of disease in monkeys exposed intranasally or by intravenous inoculation, but acutely fatal meningoencephalitis in 11 of 18 monkeys inoculated intrathecally).[20] The immune response to the challenge of Naegleria typically involves phagocyte production (neutrophils) along with the production of antibody.[21] There has been no demonstrable protective immune mechanism to this parasite, due in part to the rapid onset of death to the host.[22] Complete immunization is not possible with the use of Naegleria vaccines. Results of laboratory studies on animals have been reported to offer 6 to 88% protection.[2]

ENVIRONMENTAL PERSISTENCE

Naegleria spp. persistence in the water environment is dependent upon the temperature of that environment.[2,12,23] Optimal temperature for Naegleria spp. is reported to be 28 to 35°C.[2,23] Table 1 contains data relating environmental temperature to survival of Naegleria. As shown, this organism is isolated with much greater frequency from thermal environments, and it appears to flourish especially well in those environments that have been thermally altered by anthropogenic activity.[2,13] Thermal discharges aid in Naegleria survival during winter months.[13] Chang suggests that Naegleria is unlikely to survive in environments where the winters are too cold for the trophozoites and too long for the survival of cysts[25]; however, this fact needs further investigation. Wellings et al. have shown that during winter months, Naegleria is isolated more often from sediment samples than from the water column.[16] Cysts can be preserved in water temperatures of 0 to 19°C, but they experience rapid decline once water temperatures drop below 0°C.[25]

Table 1. Effect of temperature on Naegleria spp.

Environment	Temperature (°C)	Survival (d)	Ref.
Tap water	4	<7	23
Tap water	25-43	>42	23
Swimming pool	4	0	23
Swimming pool	25	7	23
Swimming pool	35	21	23
Filtered lake water	25	42	23
Lake water	25	7	23
Lake water	30-35	(+)[a]	16
Thermal mud	28-30	(+)[a]	11
Thermal mud	45	(+)[a]	24
Media[b]	≥ 51	≤0.024	25
Media[c]	≥ 51	≤0.086	25

[a] Positive growth of Naegleria.

[b] Trophozoites in media.

[c] Cysts in media.

Naegleria prefers an environment with a pH of 6.5 to 7.0 , but has been isolated from pH 9 environments.[13] Free-living Naegleria can survive dissolved-oxygen concentrations as low as 1.7 to 2.8 mg/L.[26] Seawater is inhibitory to Naegleria spp., although they can survive in environments containing up to 1% NaCl.[26] Chang has reported that the ameba and cyst forms of Naegleria are extremely sensitive to drying.[25] For example, trophozoites could not survive any period of drying, whereas cysts survive less than 5 min when dried (26°C, 22% relative humidity). This information contradicts the epidemiological findings relating dust to the transmission of PAM via the cysts.[17]

De Jonckheere and van de Voorde have reported that, in surveys of organically polluted waters, Naegleria apparently prefers more dilute (less polluted) sources.[13] Also, Scaglia et al. found that mud baths and therapeutic pools, which had extremely low numbers of total bacteria, harbored potentially pathogenic Naegleria australiensis.[24]

DOSE RESPONSE

No information is available on the dose of Naegleria spp. necessary to cause disease in the human host. However, based on data from the occurrences of human disease from Florida (U.S.) lakes, the estimated risk of infection by Naegleria was one in 2.6×10^6 exposures.[2] This may be a reasonable estimate for Naegleria in large bodies of water because billions of people have visited freshwater bathing areas, and the reported cases of naeglerial PAM have only occurred in less than 200 individuals.[2] However, in a relatively small body of water (i.e., a swimming pool in Czechoslovakia), 16 persons succumbed to PAM.[8] Incidents like this might affect the risk estimate.

John and Nussbaum have shown that 1×10^3 Naegleria trophozoites are necessary to infect laboratory mice.[27] Table 2 contains information relating ameba concentration and the swimming time for mice.[27] Smego and Durak found that 1×10^3 Naegleria organisms were sufficient to kill 100% of exposed laboratory rabbits, whereas 1×10^2 organisms brought about no fatalities.[7] In another study,[2] it was reported that only 10 Naegleria organisms were necessary to kill a chick embryo. Death of the embryo occurred in 5 d.

LATENCY

The typical onset of PAM due to Naegleria infection is 3 to 7 d,[3,5] although incubation periods of 1 to 14 d have also been reported.[4,5,9]

Table 2. Contact-dose of Naegleria for producing lethality in swimming laboratory mice.[a]

Concentration of amebae/mL	Cumulative dead (%) Swimming time (min)			
	2.5	5	10	20
10^2	--	0	0	0
10^3	--	0	10	10
10^4	0	10	40	40
10^5	30	40	60	70
10^6	--	70	--	--

[a] From John and Nussbaum.[27]

DISINFECTANTS

Data on the effects of disinfectants on Naegleria identified by this literature search are shown in Table 3. Of the two protozoans responsible for meningoencephalitis (i.e., Naegleria and Acanthamoeba), Naegleria trophozoites, as well as cysts, are the least resistant to halogen disinfectants.[28,31] This resistance may result from the difference in chemical composition of the cell membranes.[28]

Chang found concentration-coefficient values of 1.05 for free chlorine and 1.4 for iodine sufficient for 99.9% removal of cysts and suggests superchlorination to destroy cysts in a water source.[25] Engel et al. reported that free chlorine is primarily responsible for cyst inactivation.[29] It was also reported that the use of chlorinated cyanurates (leading to the formation of cyanuric acid) inhibited the effect of chlorine on cysts.[29] De Jonckheere described the effects of chlorine, bromine, and ultraviolet light (UV) on Naegleria in thermal hydrotherapy pools.[30] It was found that 2 mg/L of chlorine and greater than 4.0 mg/L of bromine were effective for removing all Naegleria, but that UV was not effective. Previous studies on disinfectants and Naegleria by De Jonckheere and van de Voorde[31] revealed that 0.5 mg/L free-available chlorine destroys 10^3 cysts/h at 2 mg/L, 10^3 cysts were destroyed in 15 min.

Table 3. Effects of disinfectants on *Naegleria* spp.

Disinfectant				
Chemical	Dose (mg/L)	Time (min)	Removal (%)	Ref.
Chlorine	0.22-0.6	-	0	24
Chlorine	0.79[a]	30	100[b]	28
Chlorine	0.74[a]	30	100[c]	28
Chlorine dioxide	0.25[a]	30	99.9[b]	28
Chlorine dioxide	0.25[a]	30	99.9[c]	28
Ozone	0.08[a]	30	99.9[b]	28
Ozone	0.075[a]	30	99.9[c]	28
Deciquam 222	0.025[a]	30	99.99[b]	28
Deciquam 222	0.025[a]	30	99.99[c]	28
Chlorine[d]	7.1[e]	6	99.9[f]	25
Chlorine[d]	5.2[e]	8	99.9[f]	25
Chlorine[d]	3.1[e]	12	99.9[f]	25
Chlorine[d]	1.4[e]	27	99.9[f]	25
Iodine[g]	7.1[e]	5	99.9[f]	25
Iodine[g]	5.4[e]	6	99.9[f]	25
Iodine[g]	3.4[e]	12	99.9[f]	25
Iodine[g]	1.6[e]	30	99.9[f]	25
Dichlorocyanurate	1.72[h]	5	99	29
Dichlorocyanurate	2.00[i]	5.5	99	29
Dichlorocyanurate	55.5[j]	7.4	99	29
Chlorine	2.0	-	100	30
Bromine	>4.0	-	100	30
Chlorine	0.3[k]	-	(+)[ℓ]	8

Table 3. (Continued)

Disinfectant	Dose (mg/L)	Time (min)	Removal (%)	Ref.
Chlorine	0.5	60	100[m]	31
Chlorine	2.0	15	100[m]	31

[a] Final concentration.
[b] *Naegleria gruberi*.
[c] *Naegleria fowleri*.
[d] pH 7.2.
[e] Residual halogen concentration.
[f] *Naegleria* cysts.
[g] pH 6.0.
[h] pH 5.0.
[i] pH 7.0.
[j] Initial titratable chlorine concentration at pH 9.0.
[k] pH 8.0.
[ℓ] *Naegleria* identified but % removal not quantified.
[m] 10^3 cysts in inoculum.

There has been much concern about the occurrence of *Naegleria* in swimming pools and/or bathing areas. Griffin recovered pathogenic *Naegleria* from waters with chlorine residual of $\leq$17 mg/L.[26] Likewise, in the swimming pool in Czechoslovakia mentioned previously, 16 persons succumbed to PAM, and chlorine levels of 0.3 mg/L were not sufficient to eradicate this organism.[8] Cracks in the pool with pockets of organic material presumably protected *Naegleria* from the effects of chlorine. It was not until the pool had been steam-cleaned with a 10% sodium hypochlorite solution that the organism was eliminated.

A survey of swimming pools in southern Australia concluded that, if chlorine residuals were maintained at 1.0 mg/L, 99% of pools would have acceptable bacteriological quality, and 94% would be free of *Naegleria*.[32] It was also estimated that for 90% of the pools to be *Naegleria*-free, a residual of more than 3.0 mg/L would have to be maintained.[32] Scaglia *et al*. investigated the occurrence of *Naegleria* spp. in a spa and reported that *Naegleria* spp. were isolated at chlorine levels of 0.22 to 0.6 mg/L.[24] This was probably due to the mixing of spa water with "therapeutic mud".

MONITORING METHODS

Currently, no standard methods have been developed for the monitoring of *Naegleria* spp. in water. However, it should be possible to use the same methods that were used for the isolation of *Giardia* and *Entamoeba* as outlined in Section 912 K in *Standard Methods for the Examination of Water and Wastewater*, 16th ed.[33] Examination and identification of *Naegleria* from a concentrated sample can be accomplished by standard laboratory methods.[6]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

There are no indicator organisms for free-living flagellated amebae, such as *Naegleria*. Scaglia *et al*. studied therapeutic spas and found no correlation between standard indicator organisms and the presence of *Naegleria*.[11,24] The presence of this organism is verified by its observation or isolation from the environment. However, there are reports of a possible relationship between the percentage of pathogenic and nonpathogenic *Naegleria* present in aquatic environments. For example, it has been stated by various researchers[12,13,15] that anywhere from 4 to 40% of environmental *Naegleria* isolates may be pathogenic in laboratory animals.

ENVIRONMENTAL CONCENTRATION

Few studies have monitored the concentration of *Naegleria* in environmental waters. Wellings *et al*. found that, depending upon the water source, 9 to 99% of samples from that source were positive for pathogenic *Naegleria*.[16] It was also estimated that the minimal volume of water yielding a pathogenic *Naegleria* isolate ranged from 24 to 5700 L, again depending upon the water source. This study also reported a maximum concentration of one ameba per 25 mL of lake water during hot summer months.

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CHAPTER 10. HELMINTHS: Ascaris lumbricoides

ETIOLOGY AND CLINICAL DISEASE

Ascaris lumbricoides is a nematode that can infect the human small intestine, causing a condition called ascariasis, or roundworm infection. Ascariasis is asymptomatic in about 85% of cases.[1] If present, symptoms are generally mild, but may be severe if the worm burden is high, for example, heavy transmission of the organism as a consequence of a seasonal pattern. This latter factor leads to symptoms because of exposure to masses of migrating larvae.[2] Ascaris suum, the pig roundworm, rarely infects humans.[3]

Adult Ascaris are grazers that live in the lumen of the small intestine and lay eggs into the intestinal contents. These eggs, which are quite resistant to adverse environmental conditions, are shed with the feces. The eggs develop and, if ingested by humans, will hatch into a rhabditiform (resembling the genus Rhabditis) larvae in the upper small intestine. These larvae penetrate the intestinal wall to go to lymphatic or capillary vessels, traveling via the portal circulation to the liver and then to the heart and lungs. In the lung, they break out into the alveoli, develop further, then migrate up the trachea and are swallowed, ending up in the small intestine.[4]

If symptoms occur, among the earliest is Löffler's syndrome, a pneumonitis with painful, labored breathing; cough; chest pain; fever; eosinophilia; and possible blood in the sputum. This condition lasts 10 to 12 d and is caused by the migrating Ascaris larvae.[1]

Symptoms most frequently caused by the adult worms are abdominal pain and discomfort.[5] Other symptoms include failure of children to thrive (i.e., nutritional effects), abdominal colic and cramps, visible peristalsis, anorexia, grinding of teeth, restlessness, intestinal noises, offensive stools, vomiting, diarrhea, and constipation.[6] Frequently, the first indication of Ascaris infection is the passing or vomiting of an adult worm.

The most common complications of ascariasis are Löffler's syndrome and intestinal obstruction.[2,6,7] Serious or fatal complications may be caused by the adult worms.[8] The fatality rate is about 0.02% of cases; the rate is higher in children.[1] Worms can migrate to the liver, gall bladder, or appendix, causing blockages; in rare cases, the worms perforate the bowel and cause peritonitis.[1] Eggs from migrating adults can cause granulomatous inflammation in tissues leading to peritonitis or pulmonary granulomas.[8] In unusual cases, liver abscesses can occur, as in the fatal case of a 21-month-old Brazilian child, who died of purulent peritonitis when one of many abscesses, containing several worms each, ruptured into the peritoneal cavity.[7] In the United States, two intestinal obstruction cases per 1000 occur each year in infected preschool children. Three percent of U.S. Ascaris obstruction cases result in death.[2] These numbers are much higher in developing countries. Complicated ascariasis is a significant cause of death in children 1 to 4 y old in some Third World countries.[5]

Ascaris can significantly affect people's nutrition, depending on their nutritional status and needs and their worm burden.[9] Heavy infections can limit nutrient utilization and decrease growth.[10] A significant inverse association between intensity of Ascaris infection and nutritional status in children living in poor, isolated hamlets was found in Bali, Indonesia. These children lived under poor nutritional conditions; a significant inverse relation could not be found in areas with a better diet.[11] These large worms, which can reach 40 cm in length, can interfere with nutrition by direct ingestion or absorption of intestinal contents. They can also obstruct villi and produce a protective antitryptic enzyme that can inhibit protein digestion.[9] Roundworms have been found to constitute up to 10% of a malnourished child's total body weight.[9] It has been estimated that a child harboring 26 worms may lose 10% of his or her total daily intake of protein.[1] Ascaris may possibly interfere with fat and carbohydrate digestion, and may cause malabsorption of vitamins A and C.[1,2,5] It is thought that protein malnutrition promotes worm infestation.[6,10]

Diagnosis of Ascaris infection is by identification of the eggs in feces,[1,12] or by microscopic identification of adult worms passed rectally or through the mouth or nose.[12] Drugs used in treatment of ascariasis include mebendazole, levamisole, piperazine hexahydrate or piperazine salts, and pyrantel pamoate.[12] Although some researchers recommend mass treatment of communities,[10] many complications can be precipitated by single-dosing a heavily infected person with antihelminthic drugs, particularly if not kept under observation.[6] Reinfection is common[10] in treated persons, with up to 30% occurring per month after chemotherapy.[13,14]

OCCURRENCE

Ascaris lumbricoides has a worldwide distribution.[1,7] It is the world's most common intestinal parasite, and is more prevalent in tropical and subtropical areas, especially those with soil pollution (e.g. human excreta) and poor personal hygiene.[4,6,10] Table 1 lists reported attack rates (i.e. rate of new cases). It is estimated that 700 million to 1.3 billion people are infected worldwide.[1,14] There is a high degree of association between infection by this organism and large households, overcrowded areas, poverty, and poor hygienic conditions.[5] In a study in Addis Ababa, Ethiopia, researchers found a clear increase in the incidence of Ascaris infection with decrease in family socioeconomic status.[32]

Table 1. Attack rates of Ascaris lumbricoides.

Area	Attack rate/1000	Description	Ref.
Sri Lanka	29-69	General population	5
Sri Lanka	71	Less than 15 y old	5
Sri Lanka	31	More than 15 y old	5
South Korea	464	Urban population	14
South Korea	596	Rural population	14
E. Timor, Indonesia	490	General population	15
W. Flores, Indonesia	430	General population	16
E. Bali	910	Children	11
E. Bali	720	General population	11
Alor, Indonesia	553	General population	17
Bali	910	General pop., 3 towns	18
Java, Indonesia	900	General rural population	19
Malaysia[a]	375	Ages 0-1 y old	20
Malaysia[a]	781	Ages 2-3 y	20
Malaysia[a]	500	$\geq$ Age 16, approximately	20
Malaysia[a]	640	Poor 4-6 y old	20
Malaysia[a]	25	Upper middle class 4-6 y	20
Madras, India	922	Children, fishing group	21
Madras, India	268	Children, elite caste	21
Madras, India	603	Children, general	21
Thailand	130	Laotian refugees	22
Thailand	59	Cambodian refugees	23
Thailand	7	Cambodian refugees	24
Vietnam[b]	247	Rural population	25
Vietnam[b]	508	Urban population	25
Vietnam[b]	325	Total population	25
N. Bangladesh	860-940	4-15 y old	26
N. Bangladesh	680	General population	26
N. Thailand	60	General population	27
Manila, Philippines	660	Poor, diarrheic children	28
Manila, Philippines	440	Poor, control children	29
Okpo, Burma	600	General population	29

Table 1. (Continued)

Area	Attack rate/1000	Description	Ref.
Ethiopia[c]	41	General population	30
Ethiopia[c]	62	Health center visitors	31
Ethiopia[d]	0–980	General population	11
Addis Ababa, Ethiopia	461	Preschool children	32
Enugu, Nigeria	40	1–2 y old	6
Enugu, Nigeria	740	3–7 y old	6
Enugu, Nigeria	220	8–12 y old	6
E. Kenya	280	1–16 y old	10
Benin, Nigeria	195	Patients	33
Nigeria	270	General population	34
Kenya	540	General population	14
Sukuta, Gambia	0	Infants, 6 mo	35
Sukuta, Gambia	10	Infants, 12 mo	35
Sukuta, Gambia	90	Infants, 18 mo	35
Sukuta, Gambia	120	Mothers	35
Ndola, Zambia	270	General population	36
Kumasi, Ghana	330	General population	36
Gaborone, Botswana	0	General population	36
Isfahan, Iran	857	General population	13
Iran	910	Children	37
Worldwide	250	Estimate	10,38
South Carolina	290	Outbreak	39
Virginia	100	Children	39
U.S.	27	General population	39
Maine	63	General population	39
Rhode Island	30	General population	39
Minnesota, Nebraska	33	General population	39
Kentucky	50	General population	39
South Carolina	56	General population	39
Georgia	29	General population	39
Alabama, Louisiana	28	General population	39
Bloomington, TX	63	Extended family	40

Table 1. (Continued)

Area	Attack rate/1000	Description	Ref.
Mississippi	40	Mental institution (MI) patients	41
Mississippi	0	MI, contact employees	41
Mississippi	10	MI, dietary employees	41
Mississippi	32	General population	39
New Mexico	57	General population	39
California	31	General population	39
U.S.	20	Sewage workers	42
U.S.	160	Farm workers	42
Rome province	3	Schoolchildren	43
Germany	900	Epidemic	42
Nova Scotia	281	Under 20 y old	44
Praslin, Seychelles	352	Patients, symptoms	45
Dominican Republic	95.7	General population	46
Belem, Brazil	82	Diarrheic children <6 y	47
Colombia	540	General population	14
Amazon	450-650	Acculturating tribes	48
Amazon	900-1000	Newly contacted tribes	48
Sao Paulo, Brazil	590	1-8 y old	49
Brazil	700	Xavante indians, male	50
Maracaibo, Venezuela	95	General population	51
Maracaibo, Venezuela	195	Poor children 0-12 y	52

[a] Kuala Lumpur, slum area.
[b] Mekong Delta area.
[c] Lake Zway Islands.
[d] Central Plateau.

As noted in several studies, no general sex differences appear to exist in the susceptibility or incidence of Ascaris infection.[2,10,19,30,31] In Bangladesh, boys appear to acquire infection earlier than girls; however, their infection rate appears to be less in the 4- to 15-y age bracket than that of girls.[26]

There is a marked age pattern found in persons infected with Ascaris. Generally, infection begins in young childhood and reaches a peak somewhere in the 4- to 9-y age group.[26,53] Two very different types of infection patterns are apparent in adults. One type is a decrease in incidence after about age 15 to 16,[12,15,20] and the other is for infection to remain high.[1,13] No explanation for the two different infection patterns has been found; sometimes both patterns can be found in the same country (e.g., in China). Furthermore, some studies have shown no difference in infection pattern between children from 1 to 16 y old.[10,30,44] Nevertheless, in all age groups, only a small proportion of people have substantial worm infestations.[2]

RESERVOIR

Humans are the reservoir of A. lumbricoides.[1,12] Attempts to infect other animals have been unsuccessful;[3,34] however, mild infections have been found in pigs,[8] as well as in dogs, cats, sheep, and orangutans.[14] The importance of these animal hosts as reservoirs of the disease is doubtful.

MODE OF TRANSMISSION

Eggs are released by gravid female worms and are discharged to the environment in the feces.[12] The eggs must undergo development for 3 to 4 wk in the environment before they are infective; consequently, transmission does not occur directly from person to person.[12] The most common methods of transmission are contaminated hands via contact with ova-bearing soil[2] and contaminated vegetables,[1] the latter having been fertilized frequently with night soil infected with Ascaris eggs.[8,14,25,37] Waterborne transmission is possible but generally not of great importance.[1] Flies have been shown to carry infective Ascaris eggs for indefinite periods.[54] The possibility of transmission of Ascaris eggs by windblown dust particles has been demonstrated.[1,55] The importance of these latter two modes of transmission, however, has not been determined.

Transmission increases with population density, amount of agriculture (particularly the use of night soil, which is soil fertilized with human excrement), illiteracy, and poor sanitation and cultural habits.[14] A study of a slum in Kuala Lumpur, Malaysia, showed that 95% of parents were unaware of the means of transmission of Ascaris.[20]

SUSCEPTIBILITY AND RESISTANCE

Susceptibility to A. lumbricoides infection is general.[12] Although the host may respond to Ascaris during the larval migratory stage, people are generally tolerant to the adult worms in the intestine.[14] Serious health effects from exposure to larvae are most pronounced in areas where transmission is seasonal.[2]

There may be some increase in resistance to infection in adults, as demonstrated by a decrease in infections of adults compared to children in areas of heavy contamination.[15,29]

ENVIRONMENTAL PERSISTENCE

Ascaris eggs are probably the most resistant to environmental conditions of all excreted pathogens.[1] Desiccation and higher temperatures, however, will kill the eggs.[14] For example, low ascariasis prevalence has been shown to occur in very hot, dry areas with severe winters.[5] In general, the moisture requirement of ova survival increases as the temperature increases.[56] Ascaris eggs generally will die relatively rapidly at moisture contents below 5%.[1] This level of dryness is never attained by sewage-sludge drying. Ascaris has increased survival in more oxygenated waters.[42] Urine is ovicidal and will kill eggs in 16 h; it will arrest development even at dilutions of 1:10.[1]

Temperature is the most important factor in Ascaris ova survival.[57] The thermal death point for Ascaris ova is about 54 to 55°C.[56] The eggs are known to live for more than a year at room temperature.[2] Eggs cease development at temperatures below 16°C, and the ideal development temperature is around 30°C. Fully matured eggs can survive freezing for a period of 4 y.[44]

Ova can live for up to 7 y in soil.[58] However, one study in the USSR demonstrated that 0.04 to 0.3% of ova were viable and infective after 14 y in soil.[14] Ova can live more than 90 d at 22 to 35°C in clay-type soils in the shade, or nearly 90 d at the same temperatures in sandy soils in shade or sun.[58]

Ascaris ova are not affected greatly by pH.[57] They can survive for 60 to 120 d when liming is used to raise the pH to between 11.5 and 12.[59]

Table 2 shows the effect of various simulated environmental conditions on Ascaris ova. Ascaris eggs have also been found to survive in sludge beds for 33 months under normal temperature fluctuations in a temperate climate.[57]

Table 2. Persistence of Ascaris ova under various drying conditions.[a]

Humidity (%)	Temperature (°C)	Exposure time (d)	Effect
40-50	25-30	4	Destroyed
77	22	15-20	Survived
<10	-	-	Survived[b]
Indoor drying	-	118	Survived
5.8	46	81[c]	Survived
3-4	46	81	Survived
7.9	<0[d]	104	25% viable
50	-	107[c]	6% viable
50	-	118[c]	6% viable
3.1[e]	-	-	10% viable

[a] From Ref. 56.

[b] Ascaris can survive in sludge with 10% moisture.

[c] Drying sludge.

[d] Less than 0°C one third of the time.

[e] Sludge dried in a petri dish.

The adult worm's life expectancy in the host ranges from 6 to 18 months, in general.[2] Infection with Ascaris, therefore, can be self-limiting if reinfection does not occur.

DOSE RESPONSE

Not much is known about the dose of A. lumbricoides ova necessary to cause infection. Croll et al. stated that 0.02% of larvae gaining entry to the host are estimated to survive to maturity.[13] In a study of experimental infection in human volunteers reported in 1951, Takata gave 25 Ascaris eggs (ova) containing embryonated larvae to seven subjects and observed infection in each of them.[60] In these infected individuals, 4.3 to 80% of the ova developed to adult worms. The average efficiency rate of ova development was 47%. In the seven volunteers, the number of mature worms that were found varied from 1 to 20, with an average of 11. However, this number of ova (25 eggs) ingested at one time would most likely be rare in natural circumstances.

LATENCY

The prepatent period (latent), between egg ingestion and egg production in the developed adult worm, is between 50 and 80 d,[13] averaging 2 months.[1,56] The incubation period, between egg ingestion and onset of symptoms, can vary from a few days (when larval migration symptoms may occur) to several months. In many cases, no evidence of illness occurs at all.[1]

DISINFECTION

Even at concentrations significantly above normal water-treatment levels, chlorine and chloramine are ineffective against Ascaris ova.[1]

Although there is a significant amount of sedimentation of Ascaris ova during primary and secondary sewage treatment, removal of eggs is incomplete[59] and would be more accurately described as concentration; they are not killed.[1] The degree of Ascaris ova inactivation during sludge digestion is related closely to the temperatures achieved.[56] For detailed information on the effects of several sewage-treatment methods on the removal and concentration of Ascaris ova, refer to Shephard's study on the control of human helminthiases.[56] Shephard's paper, which summarized findings of several researchers, indicates that results of studies can be conflicting and that the data must be carefully interpreted.

The 1964 World Health Organization's recommends the following conditions for treating night soil to remove Ascaris eggs: 30 d at 38°C for anaerobic digestion, or 20 d at 45°C for aerobic digestion.[56]

Septic-tank removal of Ascaris can be as high as 99.4%, with 3-d retention time, but is usually far lower than this in actual practice.[1] Waste stabilization ponds with an overall retention time of 20 d and 3 or more cells can remove Ascaris ova completely.[7] Filtration through soil or sand should remove Ascaris eggs from the leachate, but those retained in the soil matrix can remain viable for several months.[1] Heat is the most reliable method of Ascaris ova destruction. Temperatures greater than 45°C must be attained, and 50°C is preferred to assure destruction. Ovicides such as Carbathion can be used to kill Ascaris eggs. For a literature summary of ovicide experiments, see Feacham.[1]

Food suspected to be contaminated with Ascaris eggs can be rendered safe by immersing in 70 to 80°C water for 5 to 10 s or soaking in a 200-ppm iodine solution for a few minutes.[2]

MONITORING METHODS

There are no standard methods for detecting Ascaris ova in the environment. Ova have been recovered from sludge by centrifugation in sucrose-density gradients.[57] Samples from feces and other materials can be examined by direct smear, dilution egg count, or modified thick-smear techniques.[61]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

No indicator-organism/pathogen relationship has been established for A. lumbricoides ova in the environment.

ENVIRONMENTAL CONCENTRATION

Table 3 is a summary of information on numbers of Ascaris ova found in various environmental samples. One female Ascaris can lay more than 200,000 ova per day.[9,61] Some researchers estimate that this number is closer to 240,000.[14] Output per female worm decreases as the worm burden increases.[61] It is estimated that the global contamination of the soil by Ascaris eggs is 9×10^{14} eggs per day.[14]

No reports of Ascaris eggs in drinking water have been found,[1] and as stated previously, waterborne transmission is not considered to be an important route for Ascaris infection.[1]

Table 3. Ascaris lumbricoides in the environment.

Area	Amount (eggs)	Description	Ref.
Egypt	15%	Water-storage-jar samples	62
Egypt	0%	Tap-water samples	62
Ibadan, Nigeria	35%	Open-water-drain samples	63
Iran	18,000/g	Treated fertilizer	37
Iran	19,000/g	Feces	37
Aleppo, Syria	1000-8000/L	Raw sewage	37
Malaysia	3340/g	Feces, children	61
Malaysia	10,000-49,999/g	Feces, children	20
Tokyo	10-80/L	Raw sewage, 1965	56
China[a]	2.3×10^6/L	Night soil	1
China	2300/g	Septic-tank sludge	1
S. Korea	38/100 g	Vegetable[b] leaves	1
S. Korea	0.6/100 g	Carrots[b]	1
Calcutta, India	200-2130/L	Raw sewage, estimate	1
E. Germany	30-83/L	Raw sewage, 1958	56
Poland	0.8/100 g	Public beach, sand, 1969	1
S. Africa	660/L	Raw sewage, 1960	56
S. Africa	19/L	Settled sewage, 1975	1
S. Africa	0-250/g	Raw sludge	1
Puerto Rico	4/20 L	Final effluent, 1964	56
Puerto Rico	4925/20 L	Activated sludge	56
Puerto Rico	38/L	Raw sewage	56
Denver	0-1/L	River water, 1954	1
Denver	0-14/L	River water[c]	1
Denver	5-10/L	Raw sewage	1
Los Angeles	<100/g	Raw sludge, 1978	1
U.S.	6%	Irrigated vegetables[d]	1
USSR	20-48/g	Raw sludge, 1938	1

[a] Kiangsu province.

[b] Grown with soil fertilized with human excrement (i.e., night soil).

[c] Below sewage outfall.

[d] Irrigated with treated sewage (chlorinated primary sludge).

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CHAPTER 11. HELMINTHS: Dracunculus medinensis

ETIOLOGY AND CLINICAL DISEASE

Dracunculus medinensis is a large nematode, commonly called the Guinea worm. This organism causes a temporarily crippling disease called dracontiasis.[1] In a typical uncomplicated case of dracontiasis, the gravid female worm, which can be over a meter in length, lies subcutaneously in the tissues.[2] About 90% or more of the worms emerge on the legs or feet.[3,4] A blister forms at the position of the worm's head, as it prepares to discharge larvae.[1] This blister, which causes a local itching and burning, bursts preferentially when it comes in contact with water. About 5 cm of the worm extrudes from the painful ulcer produced, and then the worm releases larvae. Larvae are expelled whenever the infected part is immersed in water. These larvae are ingested by the intermediate host, Cyclops copepods, and the ingestion results in infection. Expulsion of larvae continues until the entire worm is extruded; generally about 4 wk.[2] The worm dies after the reproductive phase, making the disease self-limiting.[5] The ulcer heals rapidly if no complications are present.[1,2] The duration of incapacitation is 3 to 18 wk.[6]

Secondary infection and other complications are common with dracontiasis. Without sequelae, dracontiasis would be a painful but temporary problem. Multiple infections can occur, with up to 40 simultaneous infections reported (although this is rare), leaving the person unable to walk or work for a long time.[7] One to three worms generally emerge per season in afflicted individuals.[8] However, the site of emergence is frequently more important than numbers in terms of disability.[9] For example, emergence on the foot can affect mobility and may predispose an individual to secondary infection. Nearly half of those persons affected suffer from secondary infection,[7] which can result in acute abscess, arthritis from calcified worms in the joints, synovitis, bubo (swelling of lymph nodes in groin area), chronic ulcers, epididymo-orchitis (inflamed testes and epididymis), and fibrous ankylosis of joints and contractures of tendons; both of the latter can cause permanent disability.[8,2] In a few cases, Dracunculus has invaded the uterus, and it may cause bouts of bleeding or repeated abortion.[10] A common cause of secondary infection is breaking the worm, which then withdraws back into the tissues, taking bacteria with it or causing a tissue reaction.[8,11] Nearly 0.5% of those infected with D. medinensis are permanently disabled,[2,12] but the disease is not generally lethal.

In a Nigerian study, the degree of disability among the population was distributed as follows: mild (minimal to no discomfort), 57%; moderate (severe discomfort but mobile), 31%; and severe (severe discomfort and immobile), 12%.[11] Dracunculosis is considered to be the major preventable cause of agricultural work loss in parts of Africa.[2,13] It has a significant impact on medical, political, and social development of affected areas and is a major handicap to the development of rural communities.[6] It is the indirect cause of major crop loss in West Africa.[13]

Infection with Dracunculus medinensis is also correlated with tetanus infection.[7,14] Up to 7% of dracontiasis victims in Upper Volta die of tetanus.[5] In Nigeria, dracunculosis lesions are the third commonest portal of entry for tetanus.[7]

Dracontiasis is easy to diagnose. The lesions are characteristic, and larvae can be collected for examination from lesions by application of a cool compress.[15]

Treatment of dracontiasis is problematic. Mass treatment at this time is not feasible and is of questionable efficacy.[5,7,11] Some authorities maintain that no effective treatment is available.[16] Metronidazole and niridazole are said to expedite expulsion of the worm, decreasing the time of disability to one-half or one-third that of untreated cases.[12] Mebendazole and thiabendazole are also used.[5] In addition to this chemotherapy, wound dressing and penicillin may be used.[10]

The most common traditional treatment involves winding the worm up on a stick, a few inches per day.[5] In India, other indigenous treatments include applications of warm cow dung, hot yellow sand, and a poultice of plant leaves.[16] The utility of the latter applications is questionable, particularly in light of secondary infections.

OCCURRENCE

Dracontiasis is probably most widespread in India, with Nigeria being the next country most afflicted. Dracontiasis is also found in other parts of Africa and the Middle East.[5] The disease is endemic in seven states in India and affects a population of 10 million in that country alone.[3] Table 1 lists geographical areas reported to have endemic infection by D. medinensis.

Dracontiasis predominantly affects rural, outlying, or poorly accessible communities without a safe source of water.[7,11,17] Factors affecting its spread include scarcity of water, settlement pattern, numerous available sites of transmission, increased mobility, water contact, poor water management, wide distribution of the intermediate host (Cyclops), poverty, and ignorance.[6,13] The population at risk are people regularly using stagnant ponds or step wells for drinking water during the dry season. This risk group comprises about 44% of those inhabiting rural West Africa,[13,14] particularly farmers.[7]

Variations in infection rates between the sexes may result from differing water consumption and contact patterns.[7] Males and females are approximately equally affected in Nigeria.[6,11,18] Males appear to have a higher incidence in parts of West

Table 1. Regions where endemic infection by Dracunculus medinensis occurs.[a]

Area	Description
India	Widespread
Iran	Bordering Persian Gulf
Iraq	Western desert, Tigris, and Euphrates lowlands
Yemen	Sporadic
Saudi Arabia	Less common with introduction of tube wells
Sudan	Common in south
Uganda	Northern section
Ethiopia	A focus near Keru village
Somalia	Sporadic cases
W. and N. Africa	Widely distributed, not well documented
Portuguese Guinea	Susana zone, high incidence
Ivory Coast	Common
Ghana	Widespread
Nigeria	Common in north and west
Pakistan	Decreased since 1968 drought
Upper Volta	No further information given
Guinea	No further information given
Senegal	No further information given
Mali	No further information given
Mauritania	No further information given
Dahomey	No further information given
Algeria	No further information given
Liberia	No further information given
Togo	No further information given
Chad	No further information given
Northern Cameroon	No further information given

[a] Summarized from Ref. 8.

Africa[13] and the Great Indian Desert region of India.[4,16] Women in Northwest Ghana have a higher incidence than men.[9] Females may have a higher incidence of infection affecting the pelvic area, as noted in one investigation.[19]

Most infections occur in persons of working age.[4,5] In Kwara State, Nigeria, the greatest infection is in those over 30 y old, with children under 10 y old having significantly fewer infections.[6,14,20] In Anambra State, Nigeria, it is estimated that 40 to 90% of the adults per farming household are incapacitated with Dracunculus infection an average of 3 to 4 wk during the farming season. However, the disease is more rare in those under 4 y of age or older than 55.[14] According to a study conducted in West Rajasthan, India, the age range affected was 2 to 75 y.[4] Table 2 displays attack rates (i.e., rate of new cases) of dracunculosis reported in various areas studied.

Dracunculus medinensis has a seasonal distribution. In India, the peak incidence is in the summer, corresponding with low water level, increased numbers of Cyclops, higher water consumption, and cleaner appearance of step-well water compared to other water sources.[3]

In areas with wet and dry seasons, where ponds used for drinking water dry up annually, maximum incidence of infection occurs during the entire rainy season. In humid-climate savannah areas of Africa, where ponds do not dry up each year, infection may be apparent for up to 8 mo of the year.[2] Generally, the peak incidence coincides with peak agricultural activities.[4,13]

RESERVOIR

Humans are the reservoir of D. medinensis,[1,13] the only species of Dracunculus to affect humans. There are no nonclinically affected carriers except those in the lengthy latent stage.[10] Although D. medinensis has been found sporadically in animals, it is not known whether there are animal reservoir hosts that can maintain the infection in the absence of humans.[8]

Many species of the copepod Cyclops are invertebrate vectors for D. medinensis. These aquatic organisms are necessary for the transmission of dracunculosis.[1]

MODE OF TRANSMISSION

Dracunculosis may be the only disease transmitted exclusively by water and by the oral route.[5] People are infected by ingesting drinking water contaminated with Cyclops, a copepod, infected with D. medinensis larvae. The larvae escape the disintegrating

Table 2. Attack rates of Dracunculus medinensis.

Area	Attack rate/1000	Description	Ref.
India	49	Range 6-103 (attack rate)	3
India	50	Affected villages	12
SW Nigeria	250	Estimate, workers 15-40 y old	2
W. Africa	800	Rural males, 25-44 y old	13
Nigeria	500	Affected every other year	14
Nigeria	500-750	Anambra State, rural	14
Nigeria	<250	Anambra State, urban	14
Nigeria	800	Anambra State, pond users	14
India	2-247	Indian desert	4
W. Nigeria	192	17 villages studied	10
NW Ghana	<100	35 of 43 villages examined	9
NW Ghana	10	13 of 43 villages examined	9
NW Ghana	200-390	3 of 43 villages examined	9
India	60	General population	16
India	75	Males	16
India	47	Females	16
Nigeria	22-585	Ibadan outskirts	7
Ghana	30-280	Danfo area	7
E. Nigeria	141-691		7
NW Ghana	16	Ages 0-4	9
NW Ghana	97	Ages 20-24	9
NW Ghana	36	Ages 65+	9
W. Africa	12	Overall population	13
Nigeria	547	Kwara State	6
Nigeria	450	Kwara State	20
Nigeria	135	General population	11
Nigeria	215	Akufo area	17

copepod in the stomach or duodenum, migrate (as they develop into adults) through the internal organs, and after mating, the females (which vastly outnumber males) migrate to subcutaneous tissues where they develop to full reproductive maturity.[1] The gravid females, which are essentially a bag of embryos by this time, discharge their larvae into water in the manner described earlier and the larvae complete the cycle by invading or being eaten by Cyclops. The timing, duration, and intensity of transmission is shown to vary with type of drinking-water source, availability of alternate sources, and the rainfall pattern.[9]

SUSCEPTIBILITY AND RESISTANCE

Susceptibility is universal.[1] There appears to be no acquired immunity, and people can be infected repeatedly and by more than one worm at a time.[4,5,7,14,18] People may suffer from this disease yearly for 15 to 50 y, whereas others under the same conditions will never be afflicted.[4]

ENVIRONMENTAL PERSISTENCE

Not much is known about Dracunculus persistence in the environment. One researcher[5] has reported that larvae can survive a few months in water, whereas others have found them to survive only from 4 to 7 d.[8] The vector, Cyclops, prefers stagnant, standing water.[7] The disease is not generally transmitted via running water or from draw wells with a circumference of less than 3 m (restricting entry of water drawers).[2] Once inside the Cyclops organism, D. medinensis larvae develop best when water temperatures range from 25 to 30°C. They will not develop at water temperatures below 19°C.[2]

DOSE-RESPONSE RELATIONSHIP

A definite median infective dose has not been determined for D. medinensis.[9] The existing information was reported by Kale[11] and is chronicled below.

In Iwoge village, Southwest Nigeria, 76 to 506 Cyclops nigerianus were found per 10 L of water during the maximum transmission season (April). The infection rate in Cyclops vectors varied from 4.7 to 10.5%, with an average of just over one larva per liter of water. Researchers on this project calculated that a person may ingest an average of 75 infected copepods in a season.[11] Each of these infected copepods will contain one to three larvae. A total of only one to three worms will finally emerge. In another study, an average of 9.5 Dracunculus larvae were found in every 5 L of water.[11] It has been estimated that in regions where Drancunculus infections are prevalent humans swallow 75 to 100 infected Cyclops per year. Thirteen and one-half percent of the general population was found to be infected.[11]

LATENCY

The incubation period for dracunculosis is about one year,[2,9,11] with a range of 10 to 14 months.[7,12] An infection usually is not carried over from one season to the next in areas with distinct dry and rainy seasons.[10]

DISINFECTION

We found no information on the effect of chlorine on infected Cyclops or the free-swimming larvae of Dracunculus medinensis. However, simple filtering of water through two layers of cloth will filter out Cyclops and render the water safe from the potential presence of mature Dracunculus larvae.[2,12] It is expected that any treatment of water that will remove crustaceans will eliminate the risk of Dracunculus infection in human consumers.

Dracunculus is one of the most easily preventable and eradicable parasites known.[2,5] There are three basic ways to control dracunculosis:[10]

1. Destroy the copepod host.
2. Provide safe water or treat available water.
3. Prevent infected people from contacting and contaminating sources of drinking water.

The copepod host can be controlled through use of a predator such as Gambusia (mosquito fish), superheated steam, or a copicide such as Abate[8] or Temephos.[2] In a study in India, Temephos was found to be effective for 4 to 6 wk in reducing Cyclops levels in water.[21] A concentration of 0.5 to 1.0 mg/L of Temephos can remove Cyclops for 5 to 7 wk, as determined by another study.[2]

One method to prevent contact between infected persons and drinking-water sources is treatment of infected people, through wound dressing and antibiotics. The actual mechanism for reduction of incidence is unclear, but it may result from a decrease in infection time and an attempt to keep the dressing dry by avoiding water contact.[10] Results of a 5-y study in Nigeria using this method of disinfection are given in Table 3 and indicate a significant reduction in cases.

Table 3. Effect of wound dressing and penicillin on Dracunculus medinensis incidence.[a]

Year of study	Incidence (%)[b]
0	19.2
1	12.0
2	5.9
3	2.5
4	0.4
5	0.1

[a] In this 5-y study,[10] lesions from D. medinensis were treated by dressing the wound and administering penicillin for secondary infection. The treatment area was monitored to detect if this action decreased incidence.

[b] Defined as percent of general population infected with Dracunculus medinensis.

According to some researchers, the best way to eradicate dracunculosis is through health education and the provision of safe water supplies.[6,11] For instance, in a severe outbreak of the disease in Kwara State, Nigeria, the villagers were unaware of the mode of transmission of Dracunculus.[20] This lack of awareness is common.

MONITORING METHODS

The typical methods for recovering Cyclops from water include filtration of the water by a plankton net,[14] funnel net,[21] or some other filtering device.[9] Cyclops are identified and dissected under a dissecting microscope in search of Dracunculus medinensis larvae.[21] A chill-coma method[14] or dilute HCl can be used to clarify the larvae for easier observation.[9]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

An indicator-organism/pathogen relationship for Dracunculus medinensis has not been identified. As is discussed below, the distribution of Dracunculus in the environment varies widely.

Table 4. Concentration of Cyclops organisms in water and corresponding percentage of Cyclops organisms infected with Dracunculus medinensis.

Area	Cyclops (organisms/volume of water)	Infected[a] (%)	Ref.
Nigeria	9.5/5 L water	-	11
Nigeria[b]	88/L	5%	20
India[c]	16-142/dip[d]	-	21
India[e]	236-736/dip[d]	-	21
India[f]	313.3/dip[d]	-	21
Nigeria[g]	16.5/2 L	0	14
Nigeria[h]	72/2 L	12.5%	14
Nigeria[i]	153/2 L	22.5	14
NW Ghana[j]	0.3-104.6/L	0.5-33.3	9

[a] Defined as percent of Cyclops organisms in sample infected with D. medinensis.

[b] Kwara State.

[c] Andhra Pradesh, draw wells.

[d] Dip = an undefined volume obtained when a net was dipped in water to gather sample.

[e] Rajasthan, step wells.

[f] Andhra Pradesh.

[g] Anambra State, draw wells.

[h] Anambra State, stream.

[i] Anambra State, pond.

[j] Pools, ponds.

CONCENTRATION IN THE ENVIRONMENT

Cyclops copepods thrive in standing water; they are not found commonly in flowing streams.[7] They also tend to sink to the bottom of a water body.[8] These factors, along with their seasonality, affect the calculation of the numbers of Dracunculus in the environment. Table 4 summarizes the available data on the concentration of cyclops in the environment, including the frequency of their infection.

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CHAPTER 12. HELMINTHS THAT CAUSE SCHISTOSOMIASIS: Schistosoma mansoni, Schistosoma japonicum, Schistosoma haematobium, Schistosoma mekongi, and Others

ETIOLOGY AND CLINICAL DISEASE ASSOCIATED WITH Schistosoma spp.

Schistosomiasis is caused by a trematode (blood fluke) Schistosoma spp. Three species are responsible primarily for the majority of schistosomiasis: S. mansoni, S. haematobium, and S. japonicum. However, in some geographical locations, S. mekongi and S. intercalatum have been implicated in human infections.[1-3]

Schistosomiasis results from the invasion of the skin by a specific waterborne, motile larvae (cercariae) of the Schistosoma organism, followed by eventual migration to major organs and other tissues.[2,3] Once the larvae enter the body, they locate in the lungs, where they mature and mate. The fertilized female then deposits eggs that develop in the hepatic portal regions of the liver and mature in the mesenteric veins of the host.[1,2] From here the eggs find their way to the intestine and are then excreted in the feces or urine, as in the case of S. haematobium.

The degree and prepatent (latency) period of symptomology is dependent upon the degree of exposure. Exposure to large numbers of Schistosoma spp. may result in variable "worm burdens" of light (<100 eggs/(g • d) of feces) to heavy (>400 eggs/(g • d) of feces) infections.[1,3]

The major pathological effects of schistosomiasis result from chronic infection in which there is major organ involvement.[2] Acute symptoms of the early stages of infection of the lungs, liver, and intestines are characterized by fever, malaise, urticaria, eosinophilia, abdominal discomfort, diarrhea, weight loss, cough, slightly enlarged liver, and sometimes an enlarged spleen.[2] The onset of chronic disease symptomology depends upon the degree of infection, and the disease results in weight loss, anemia, symptoms referable to the intestinal tract, splenomegaly, fibrosis of the liver, and ascites.[2] Schistosomiasis may also be manifested in a much less virulent form known as Katayama syndrome. This condition results from light infections with low worm burden.[4] Cerebral infections have been reported, but occur only with S. japonicum.[2,3] Concomitant infections do occur with Entamoeba histolytica in those persons with schistosomal polyposis.[5] Also, Melhem and LoVerde have shown that Salmonella typhimurium adhere to the schistosomula and can prevent adequate treatment of salmonellosis.[6]

Schistosomiasis may persist for many years. From a study in Puerto Rico, Hiatt et al. have estimated a half-life of 23 y for S. mansoni.[7] Other studies have reported persistence of 5 to 30 y.[8,9] Sqeed indicates that the duration of schistosomiasis ranges from months to years, depending on treatment.[10]

The drug of choice for the treatment of schistosomiasis is Praziquantel.[1] Oxamniquine has been shown to produce a 70% cure rate for S. mansoni.[11]

OCCURRENCE OF Schistosoma mansoni AND Schistosoma japonicum

Table 1 contains the occurrence data identified by our literature review for schistosomiasis resulting from S. mansoni and S. japonicum. Generally, S. mansoni is distributed throughout Central Africa, the Arabian peninsula, Brazil, Surinam, Venezuela, and some Caribbean Islands.[1,3] Schistosoma japonicum is found in East Asia, especially in China, Japan, Philippines, Celebes, Southeast Asia, and Indonesia.[1,3]

Within these populations of infected individuals are subpopulations of varying degree of infection. For example, a survey of Yemeni immigrants to the U.S. revealed that up to 50% of the immigrants were infected; and of this group, 50% suffered from a light infection, 27% from a moderate infection, and 16% from a heavy infection.[8]

Some of the information presented in Table 1 may be outdated because, in many countries, control programs have been instituted. For example, on the Caribbean island of St. Lucia, the incidence of schistosomiasis was cut by 92% in those areas where plumbing was added.[12] Other control methods included eradication programs of the intermediate host (i.e. snail).[12,13,24,25] However, even with these methods in these areas, without the education of the inhabitants in proper sanitation practices, schistosomiasis will likely persist.[28]

RESERVOIR FOR S. mansoni AND S. japonicum

Two vital hosts are needed for the propagation of schistosomiasis: the human and the snail.[1] Schistosoma mansoni relies on the presence of the snail of the genus Biomphalaria as an intermediate to human infection.[1,3] Schistosoma japonicum relies on the snail of the genus Oncomelania; however, the adult trematode of S. japonicum has been found to reside in mammalian hosts other than humans, such as dogs, cats, pigs, cattle, horses, wild rodents, and water buffalo.[1,26,27] Recently, Fuller et al. have attributed the presence of S. mansoni cercariae in Ethiopian rivers to monkeys and baboons.[29]

Table 1. Occurrence of Schistosoma spp.

Schistosoma spp.	Location	Incidence[a]	Infection Light[b]	Infection Moderate[c]	Infection Heavy[d]	Ref.
S. mansoni	Immigrants[e]	560	56	27	17	8
	Puerto Rico	400[f]				7
	Puerto Rico	350[g]				7
	St. Lucia, Carib.	202[h]				12
	St. Lucia, Carib.	126[i]				12
	St. Lucia, Carib.	52[j]				13
	St. Lucia, Carib.	38[k]				13
	West Australia[ℓ]	30				9
	Kenya	470	26	15	6	14
	Zambia[m]	100–220				15
	West Sudan[n]	560				10
	Sudan[o]	570				16
	Tanzania	347	52	39	9	17
	Ethiopia	540[p]				18
	Ethiopia	150[q]				18
	Ethiopia	100[r]				18
	Ethiopia[s]	450	100			4
	Ethiopia	320				19
	Yemen	290[t]				20

[a] Infected population per 1000 individuals.

[b] Light infection = <100 eggs/g feces.

[c] Moderate infection = 100 to 400 eggs/g feces.

[d] Heavy infection = >400 eggs/g feces.

[e] Immigrants from Yemen to California.

[f] Reported at the beginning of schistosomiasis control program.

[g] Reported at the end of schistosomiasis control program.

[h] Nontest area.

[i] Plumbing installed to some residents.

[j] High-transmission area.

[k] Low-transmission area.

[ℓ] Reported cases in Polish immigrants from Africa.

[m] In children, 0–10 y old.

[n] In European visitors.

[o] Migrant workers.

[p] Measured in individuals that wade in water.

[q] Measured in individuals that wash with water.

[r] Fetching and carrying water.

[s] American tourists on raft trip down the Omo River.

[t] Estimated that one million of total population is infected.

Table 1. (Continued)

Schistosoma spp.	Location	Incidence[a]	Infection: Light[b]	Moderate[c]	Heavy[d]	Ref.
S. japonicum	Philippines[u]	≤500	17-30	7-14	2-7	21
	Philippines[v]	320	21	8	3	22
	Philippines[w]	165				23
	Japan	253[x]				24
	Japan	96[y]				24
	China	<500[z]	10	5	3	25
	Laos	144				26
	Thailand	18				26
	Indonesia	100-700				27

[u] Reported for the year 1983.

[v] Reported for Leyte Island in 1980.

[w] Reported for the year 1976.

[x] Interdermally tested.

[y] Stool examination.

[z] Represents number of population treated. It is estimated that 25% have been treated repeatedly.

MODE OF TRANSMISSION OF S. mansoni AND S. japonicum

Schistosoma spp. are acquired by humans by direct contact with water containing the larval form (cercariae) of the Schistosoma organism.[1,3] The cercariae are thought to be attracted to the human by negative phototaxis (cercariae move toward shadowing)[30] and chemotaxis (chemicals on the skin stimulate movement toward chemical source).[31] The cercariae penetrate the skin, make their way to the lung, and then proceed to the liver. Once in the liver, S. mansoni and S. japonicum reach maturity (schistosomula) and migrate to the mesenteric veins, where they remain. From this point, the schistosomula deposit eggs, which are excreted from the body in the feces. If the eggs enter water, they are stimulated to hatch and release larvae, or "miracidia," which seek out the specific snail host. In the snail, the miracidia develop into cercariae after several weeks and are released back into the water where they can infect a mammalian host.[1-3] Upatham has reported that standing water facilitates Schistosoma spp. cercariae infection by 50% more than running water.[32] See further discussion in section on Environmental Persistence.

SUSCEPTIBILITY AND RESISTANCE TO S. mansoni AND S. japonicum

Susceptibility to Schistosoma spp. is universal.[1,2] Resistance is variable and poorly understood. In most instances with S. mansoni and S. japonicum, children and young adults (12 to 24 y old) are more susceptible; however, as the individuals grow older, the incidence declines slightly.[7,14,16-18,33] Recently, Sturrock et al. have proposed that humans are more likely to be exposed to several light infections rather than to single large challenge doses.[34] In fact, results from this study have shown that a series of small exposures conferred some resistance to larger challenges. However, the development of vaccines is complicated by the different antigenic forms the organism can take in humans, and work in this area is being pursued vigorously.

ENVIRONMENTAL PERSISTENCE OF S. mansoni AND S. japonicum

Schistosoma spp. are linked directly to water due to the two larval stages (cercariae and miracidia) in the life cycle; the intermediate host is an aquatic, freshwater snail (except for Oncomelania, which are amphibious).[2,3]

Upatham has reported that S. mansoni cercariae do not survive as long in running water as in standing water.[32] This study indicated that in laboratory mice, maximum infection occurred at stream velocities of 39 cm/s. Also, because the cercariae rely on chemotaxis and negative phototaxis to locate the host, higher infection rates (50%) occurred in laboratory mice in standing water.[32] Generally, cercariae survive for about 48 h in fresh water.[3]

Prah and James have shown that because miracidia are sensitive to ultraviolet light, they survive longer in turbid water.[35] Miracidia were found to retain infectivity for about 9 to 12 h at 5 to 10°C, 9 to 12 h at 18 to 30°C, and 6 to 9 h at 35 to 38°C.[35] The maximum survival time reported for miracidia in water was 16 h at a water temperature of 15°C.[36]

The environmental conditions on the island of Leyte in the Philippines, where schistosomiasis is an endemic disease as a consequence of the presence of S. japonicum, consist of (1) 252 cm/y of rainfall; (2) a mean temperature of 26°C (25 to 28°C range); and (3) 83% humidity.[37]

DOSE RESPONSE ASSOCIATED WITH S. mansoni AND S. japonicum

We found no information concerning the dose-response relationship between S. mansoni or S. japonicum and diseased humans. There is, however, some information dealing with animal models in vivo as well as in situ.

Sturrock et al. have proposed that humans most likely experience many light infections to S. mansoni, which are due to low doses.[34] Exposing baboons to low doses over a period of time (10 cercariae/(animal•wk) resulted in the recovery of only 21% of the infecting cercariae as worms from the animal host. However, in a single challenge experiment (2500 cercariae/animal), 78% of the infecting cercariae were recovered as worms from the host.

Upatham exposed mice that normally swim in canals to different concentrations of S. mansoni in water that was moving at different flow rates.[38] It was reported that in flowing waters (27 to 37 cm/s) 26 cercariae/L were needed to infect the mice, but in rapidly flowing streams (76 cm/s), infections were less likely to occur.

LATENCY PERIOD FOR SCHISTOSOMIASIS PRODUCED BY S. mansoni AND S. japonicum

The latency period for schistosomiasis, or the time it takes for the disease to develop into severe acute systemic manifestations, may be as long as 2 to 6 wk, both before and after the initial deposition of eggs.[1,2] According to one report, an American tourist developed symptoms 4 y after returning from Kenya.[39]

DISINFECTANTS AGAINST S. mansoni AND S. japonicum

Methods for control of schistosomiasis center on the destruction of eggs, host snails, and the larval stages (cercariae or miracidia), and on education.

Rowan has shown that free-swimming miracidia were killed easily by 0.2 ppm chlorine under the following conditions: 30 min contact time, pH 7 to 9, and a biochemical oxygen demand (BOD) between 20 and 46 mg/L, whereas miracidia eggs require 0.5 to 0.85 ppm chlorine.[40] This information and previous studies[3] have demonstrated that primary sedimentation will remove 80% of S. mansoni eggs, and trickling filter or activated sludge can remove 99.5 to 100% of these eggs.

Coles and Mann were able to achieve complete elimination (100% removal) of S. mansoni cercariae with 0.5 ppm chlorine for 30 min.[41] Optimum pH for disinfection was 5.5, and as the pH was increased to 8.5, it took longer to eliminate the cercariae. Schistosoma japonicum cercariae are reportedly destroyed completely with 1.0 ppm chlorine within 30 min.[41]

Prah and James have demonstrated the sensitivity of S. mansoni miracidia to ultraviolet (UV) light.[35] After 30 s of irradiation at 2540 Å, infectivity rate declined 12%; after 40 s of irradiation, the infectivity rate declined 22%. Because UV light can only penetrate 15 cm in clear, clean water, turbid water will protect the miracidia from disinfection by UV.

Many communities have instituted antisnail programs, which include the use of molluscicides and the cleaning of drainage canals.[22,42] The major problem with this method is that it must be continued over long periods of time, as the adult worms may survive for many years in the human host.[3]

In a 5-y control program in a Puerto Rican community, the molluscicide, niclosamide, was used to remove Biomphalaria glabrata from swamps and streams.[7] The snail was all but removed, but the prevalence of disease in the community declined by only 3 to 6%. This same study indicates that infected snails are found present toward the end of the dry season and for about 1 to 2 months after it rains. Teklehaimanot and Goll found that, in Ethiopia, snail populations peaked in the months of March through June.[42] It was suggested that the molluscicides should be applied before the rains begin and near the end of the irrigation season. More recently, Goll et al. used Endod to control snails in the Mai Shanna River, Ethiopia, and the prevalence of disease in the community dropped from 61.5 to 36.4%.[19] A snail eradication program in Sudan brought about mixed results.[16] The prevalence rate in migrant "westerners" was reduced in treated areas; however, this was not the case in Arab nomad populations. The molluscicide, Clonitralide, was employed in a 10-y control program on St. Lucia Island in the Caribbean Sea.[13] This program resulted in a 92% reduction in the prevalence rate. Also, with the installation of plumbing, the disease-morbidity prevalence rates were decreased by 13 to 60% during a 3-y period in this same program.[43]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP FOR S. mansoni AND S. japonicum

The standard bacteriological indicator organisms used for fecal contamination are not useful for predicting the presence of cercariae. Although the presence of miracidia may be an indicator of recent fecal pollution, cercariae emerge from snails several weeks after the miracidia are introduced.[3] Therefore, the presence of the infected host snail is probably the best indicator of cercariae.

Prior to the institution of a control program on St. Lucia Island for the Biomphalaria snail, the infection rate of snails harboring cercariae was 5%.[44] A follow-up survey of the infectivity rate in the same snail population following a 10-y molluscicide program revealed that only 0.06% of the snails were harboring S. mansoni.[13]

Ito et al. found up to 48% of the snails, Oncomelani quadrasi, surveyed in the Philippines were infected with cercariae.[45] Most of these cercariae were of S. japonicum; however, some were thought to be a new species. On the island of Taiwan Kuntz found that one out of every 2500 snails contained the cercariae of S. japonicum.[46]

ENVIRONMENTAL CONCENTRATION OF S. mansoni AND S. japonicum

The environmental concentration of Schistosoma spp. is difficult to define because of the three different stages that exist in the environment: excreted eggs, miracidia, and cercariae. Both the miracidia and the cercariae are free-swimming and do not survive long in the environment; however, snails and humans can provide a constant source of these organisms.

The amount of eggs released by humans depends upon the severity of the infection (worm burden). Infection by Schistosoma japonicum can result in the passage of up to 3500 eggs/d, whereas infection by S. mansoni may lead to the passage of up to 300 eggs/d.[2] Light infections are characterized by the shedding of <100 eggs/g feces daily; moderate infections yield 100 to 400 eggs/g feces daily; and heavy infections yield >400 eggs/g feces daily. One survey of the microbiological quality of open drains in Ibadan, Nigeria, found that 37% of the samples taken from these drains were positive for S. mansoni miracidia.[47]

The number of cercariae excreted from the snail host depends upon the Schistosoma spp. as well as the snail species involved.[3] For example, approximately 12 S. japonicum cercariae can be excreted per day over several months by the amphibious snail, Oncomelania quadrasi; whereas, the aquatic snail, Biomphalaria glabrata, excretes thousands of S. mansoni cercariae daily (although the Biomphalaria snail survives only about 2 wk).[3] Upatham found 0.05 to 21 S. mansoni cercariae/L in habitats harboring Biomphalaria glabrata.[44]

ETIOLOGY AND CLINICAL DISEASE ASSOCIATED WITH Schistosoma mekongi

Schistosoma mekongi is a blood fluke that is closely related in morphology and disease symptoms to S. japonicum.[48,49] Differentiation is based upon parasite egg morphology, snail host, and geographic area of occurrence.[50,51] Relatively little is known about S. mekongi, which was only thought to differ from S. japonicum as recently as 1968.[50] The disease produced by S. mekongi is difficult to differentiate, on a clinical basis, from S. japonicum.[50] The infection can be effectively treated with praziquantel.[52]

OCCURRENCE OF S. mekongi

Schistosoma mekongi is found in Southeast Asia along the Mekong River from Pakse, southern Laos, to Khong Island, Laos, and as far south as Strung Teng and Kratie, Cambodia. Areas west of the Mekong in Thailand and Cambodia are also infected with this schistosome. In fact, isolated cases have been reported from Malaysia, Southern Thailand, and Java, Indonesia.[51] The morbidity data for this disease and its relationship to geographic region appear in Table 2.

RESERVOIR FOR S. mekongi

Whether animals can be reservoirs for Schistosoma mekongi to the extent that they are for S. japonicum has not been determined (see Reservoir section for S. japonicum). At present, only dogs and humans are known to be naturally infected by S. mekongi.[49]

The snail host for S. mekongi has been identified as Tricula aperta.[51] To date, efforts to infect Oncomelania snails (the host for S. japonicum) have failed.[49]

MODE OF TRANSMISSION FOR S. mekongi

Schistosoma mekongi is transmitted to both snail and definitive hosts by water. The miracidia of S. mekongi develop into cercariae in Tricula aperta snails. The population of this snail is reported to have a seasonal peak between May and June at Khong Island, Laos.[57] The aquatic cercariae invade any skin or mucosa that come into contact with the water.[48] Schistosoma mekongi infections can occur in moving water, in contrast to S. japonicum.[57] However, the life cycle appears to be similar to that of S. japonicum.[49]

Table 2. Attack rate[a] of Schistosoma mekongi.

Area	Attack rate/1000	Description	Ref.
Cambodia[b]	70-100	Fishermen[c]	50
Cambodia[b]	140-220	Children[c]	50
Cambodia[d]	36	General population	50
Cambodia[e]	8	General population	50
Thailand	30	Cambodian refugees	53
Thailand	2.2	22,500 Laotian refugees	54
N. Thailand	15	General population	55
Thailand	170	Cambodian refugees	56

[a] Attack rate is equivalent to the rate of new cases of the disease.

[b] Kratie, Cambodia.

[c] Ethnic Vietnamese fishermen who live on boats along the Mekong River.

[d] Strung Teng, Cambodia.

[e] Lower Mekong River, Cambodia.

SUSCEPTIBILITY AND RESISTANCE TO S. mekongi

Information on the susceptibility or resistance of humans to S. mekongi is not available.

ENVIRONMENTAL PERSISTENCE OF S. mekongi

Information on the persistence of S. mekongi in the environment is not available.

DOSE RESPONSE ASSOCIATED WITH S. mekongi

No information is available on the infective dose of S. mekongi in humans. Tables 3 and 4 display information on infection studies in animals.

Table 3. Experimental infection of animals with Schistosoma mekongi.[a]

Animal	No.	No. cercariae/animal	No. worms recovered	Prepatency[b] (d)
Dog no. 1	1	124	not determined	49
Dog no. 2	1	214	not determined	46
Mice	2	40	not determined	46
Hamsters	5	100	37[c]	43
Rabbits	2	64	-[d]	-

[a] From Ref. 58.

[b] Prepatency is defined as the existence of the organism in an unobserved state (i.e., latent).

[c] One hamster was examined for worms; 24 males and 13 females were found.

[d] No adult worms were found in either rabbit; however, schistosome eggs were found in one of the animals.

Table 4. Infection of white mice with Schistosoma mekongi following exposure to water from the Mekong River, near Khong Island, Laos.[a]

Date	Exposure (h)	No. of animals surviving[b]	No. of animals infected with worms	No. of worms per infected animal
4/71	15	26	0	0
4/72	40	10	9	7-23
4/72	40	8	2	2-5

[a] From Ref. 57.

[b] Number of experimental animals remaining alive after 46 d.

LATENCY PERIOD FOR S. mekongi

In experimental animals, the latency period for S. mekongi is 43 to 49 d. This time period is shorter than that of S. japonicum.[49,58]

DISINFECTION FOR S. mekongi

According to the literature that we have reviewed, there is no information available regarding the disinfection of S. mekongi from water.

MONITORING METHODS FOR S. mekongi

No specific monitoring methods have been developed for S. mekongi. In general, methods available for the identification of other schistosomes should be adequate for the identification of S. mekongi.

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP FOR S. mekongi

No relationship has been reported to exist between microbial water-quality indicators and the presence of schistosome cercariae or the incidence of the disease.

ENVIRONMENTAL CONCENTRATION FOR S. mekongi

There is a paucity of information on the environmental concentration of S. mekongi. In a 1971 to 1972 study at Khong Island, Laos, the natural snail infection (percentage of exposed snails with endemic infection) was calculated at 0.3 to 0.16% of the population. When induced to shed cercariae, these infected snails released 2 to 20 cercariae per day.[57]

ETIOLOGY AND CLINICAL DISEASE ASSOCIATED WITH Schistosoma haematobium

Schistosoma haematobium is the causative agent of vesical or urinary schistosomiasis.[1,2] The adult blood flukes live in the veins around the urinary bladder.[1] As with the other schistosomes, symptoms differ with acute and chronic exposure. Acute symptoms are reactions to the immature and adult flukes; they occur, if at all, during the time of initial exposure. The most common symptoms of S. haematobium-induced acute schistosomiasis (also known as Katayama fever) are fever, cough, diarrhea, pain in the joints, loss of appetite, malaise. and hives associated with leukocytes and eosinophilia.[59] Pulmonary involvement from migrating immature flukes may occur.[2]

Chronic symptoms primarily are present as an inflammatory response to the eggs of S. haematobium that become deposited in the bladder submucosa, mucosa, and blood vessels.[2] Commonly, these include hematuria and painful urination, as well as the symptoms of acute schistosomiasis, which decrease in intensity over time.[59] More advanced lesions include partial blockage of the ureters with the possibility of kidney damage, urinary stones,[3] hepatomegaly,[60] and renal and bladder changes.[61] A cytoscopic study of children, 5 to 12 y old, living in Middle Egypt found the following kidney and bladder lesions (in order of decreasing frequency): hyperemia, sandy patches, tubercles, ulcers nodules, and polyps.[62] The combined toxic, chemical, and mechanical irritation from vesical schistosomiasis apparently predisposes the infected person to malignancy. Urinary schistosomiasis is considered to be the most common cause of bladder cancer in male agricultural workers in Egypt.[2]

Lesions are found even in persons with very low egg counts in the urine.[61,63] In light infections, symptoms may not show up for several years. After hematuria, the most characteristic symptom observed is painful and frequent urination, often with mucus and pus in the urine. This condition can be followed by loss of bladder elasticity and a resulting incomplete micturition. Temperature may elevate daily, with sweating, malaise, weakness, and dull pain in affected areas. Cystitis is progressive with secondary infection common.[2] In all degrees of infection (heavy, moderate, and light) the aforementioned symptoms may be found. Many other symptoms occur but are less common.[2] Lesions are reversible if the infection is treated soon enough.[64]

Schistosoma haematobium is relatively susceptible to chemotherapy. Infection by S. haematobium can be treated with metrifonate, niridazole, praziquantel, or antimony dimercaptosuccinate.[2]

OCCURRENCE OF S. haematobium

Schistosoma haematobium is found throughout most of Africa and in the Middle East,[1] with small foci in India.[3] Frequently, a difference in attack rate (i.e., rate of new cases) is apparent among the sexes, but this is probably due to activity differences imposed by the various local cultures.[65] For example, males are reported to have a higher incidence in Nigeria,[66,67] Mauritania,[68] and Upper Egypt.[69] A study in Kenya, however, showed no difference in infection rate between boys and girls.[61] Additionally, females were found to have higher infection rates than males in eastern Sierra Leone.[70] Further complicating matters with regard to difference in attack rate among sexes is a report that adult females in Gambia have a higher exposure to infection, but lower prevalence than males.[71] Moreover, in some countries the incidence in females is not possible to ascertain because of the cultural seclusion of women.[69,72]

A sharp peak in prevalence and intensity of urinary schistosomiasis in school children has been found; however, this prevalence and intensity decreases with age.[69] Generally, a peak is noted at around ages 10 to 15, with a gradual decline stabilizing between the ages of 30 and 40.[71] This peak followed by a decline has been attributed to acquired immunity, changes in the pattern of water contact, or a combination of both factors.[69] However, reasons for the change of prevalence with age remain a subject of debate.[69,71,73-75]

Schistosomiasis is one of the few infections that is still spreading steadily and increasing in intensity.[3,74] This persistence is due in part to development of various water-resource projects.[65,68] Nevertheless, in some areas, where water-resource development is occurring, such as northern Nigeria, the disease incidence is decreasing because of schistosomiasis-reduction programs.[65] Such active reduction programs have achieved a certain amount of success,[76] and although it is doubtful that schistosomiasis can ever be eradicated, several approaches to control can reduce disease transmission. For example, snail-host numbers can be reduced through the application of molluscicides and by habitat modification. Humans infected with S. haematobium can be treated with several effective drugs now available. Host-water-parasite contact can also be reduced through effective water-delivery design or modification and through sanitation.[76] Table 5 summarizes attack rates (i.e., rates of new cases of the disease) of S. haematobium around the world.

RESERVOIR FOR S. haematobium

Humans are the principal reservoir for S. haematobium. Schistosoma haematobium has been found in a few baboons.[90] An appropriate snail host must also exist in an area for the trematode to persist.[3] The usual snail hosts for S. haematobium larvae are in the Bulinus and Physopsis genera.[2]

MODE OF TRANSMISSION OF S. haematobium

Urinary schistosomiasis infection is transmitted by water that has been contaminated by urine containing the schistosome eggs.[2] The eggs subsequently hatch, producing an intermediate larval form known as a miracidium, which infects susceptible

Table 5. Attack rate of Schistosoma haematobium.

Area	Attack rate per 1000 Range	Average	Description	Ref.
Swaziland	151-358		Farm workers	76
Swaziland	64-379		Children	76
Middle Egypt		353	Children 6-10 y	62
Southern Egypt	239-640		6 villages	74
Coastal Kenya		840	School children	61
Tanzania		155	Undeveloped area	77
Kenya		190	General population	63
Liberia		227	General population	78
Nigeria		240	Ages 6-15 y	67
Nigeria		343	Males 6-15 y	67
Nigeria		115	Females 6-15 y	67
Malawi		1000	Children, some areas	79
Zambia		180	Piped-water source	80
Zambia		680	High-incidence area	80
Upper Egypt	716-816		Children 5-16 y	69
Upper Egypt		260	General population	69
Egypt		130	Teenagers	60
Somalia	90-1000	600	General population	81
Somalia	272-581		Undeveloped area	81
Somalia	587-756		Water-developed area	81
Saudi Arabia[a]		6	Males, primarily	72
Saudi Arabia	18-140		Males	72
Saudi Arabia		500	Males	72
Saudi Arabia		312	Males	72
Saudi Arabia		0	Males	72
Libya		53	School children	82
Libya		24	General population	82
Kenya[b]		35	School children	83
Kenya[b]	300-525		School children	83
Upper Egypt[c]		194	Students 5-16 y	69
Upper Egypt		98	Students 5-16 y	69
Upper Egypt		361	Males	69

Table 5. (Continued)

Area	Attack rate per 1000 Range	Attack rate per 1000 Average	Description	Ref.
Upper Egypt		183	Females	69
Mauritania		410	Males 7-10 y	68
Mauritania		240	Females 7-10 y	68
Mauritania	140-780		Children 10 y	68
Mauritania	310-400		Overall estimate	68
Northern Nigeria		550	Males 15 y	66
Northern Nigeria		240	Females 15 y	66
Ethiopia, marshy	60-520		Seminomadic	84
Ethiopia, marshy	0-270		Agricultural group	84
Sierra Leone[d]	70		Pupils	85
Yemen	45-719	340	General population	86
Liberia		480	School children	87
Liberia		160	School children	87
Tongaland		688	School children	88
Sierra Leone		82	General population	70
Mahashtra, India		6.6	General population	89
Northern Nigeria		250	Males 25 y	66
Northern Nigeria		80	Females 25 y	66

[a] The five listings for Saudi Arabia are for the following areas, respectively: north-central, western, southwestern, northwestern, and south-central.

[b] The two listings for Kenya are of the Kano plain and the Kano-plain border area, respectively.

[c] The first two listings for Upper Egypt are of students living near canals and farther from canals, respectively.

[d] Sierra Leone, reportedly, is a nonendemic area for S. haematobium.

snails. In the snail, the miracidium experiences a propagative development with the formation of free-swimming larvae, known as cercariae. These cercariae emerge from the snail hosts and penetrate the skin of persons in contact with infected water.

Urinary schistosomiasis has a seasonal peak, generally during warmer, drier periods.[91] Production of cercariae by snails can become nearly dormant in areas with cool winters.[91] The period of highest cercarial shedding by snails, early summer, frequently coincides with the season of peak water contact by humans.[69]

Rivers and canals are implicated as transmission sites less frequently than standing water such as swamps, ponds, and lakes.[69,84] Until recently, a water-flow speed of 70 to 100 cm/s was considered too fast for effective transmission of the cercariae, but this belief has been disproved.[69]

In northern Nigeria, a Muslim area, males are responsible for 98% of contamination and exposure activity.[66]

SUSCEPTIBILITY AND RESISTANCE TO S. haematobium

Generally, it is believed that some immunity to schistosomiasis develops over time. Evidence for the development of immunity is the fact that variations in egg output with age have been documented, and these variations cannot be explained adequately by changes in water contact alone.[69,74,75] Egg output and egg hatchability also decrease with increasing age,[66] also suggesting partial immunity. Further evidence of acquired immunity comes from one 3-y study[75] that found the amount of acquisition measured by egg count in middle-aged persons was 1000 times less than that measured in children 5 to 7 y old. Also, it was shown that protective immunity may be more active at ages 30 to 40 than at ages 10 to 20, and that continuing exposure to cercariae may be important for maintenance of immunity.[75] Other investigators report that acquired immunity is not developed, and the variations with age are due only to water-contact changes; these researchers currently are in the minority.[73] However, the data suggest that the existence of immunity is incomplete at best.[3]

Partial immunity, developed after chemotherapy, has been shown to prevent reinfection for a few months.[60] Another factor that may aid the development of immunity is the exposure to bovine schistosomes, which are not pathogenic to humans but which may bring about an immune response that can interfere with S. haematobium development. Exposure to bovine schistosomes has been shown to result in the lower pathogenicity of S. haematobium in populations living in western Kenya as compared to those living on the coast of Kenya, where bovine schistosomes are not endemic.[61]

Protective immunity in animals has been well studied and well documented.[59] However, based on the previous information, human immunity to schistosome infections remains controversial.

ENVIRONMENTAL PERSISTENCE OF S. haematobium

Miracidia and cercariae of S. haematobium are fragile and must find a snail or vertebrate host, respectively, in a matter of hours or they will not survive.[3] Water temperature or the amount of UV radiation from the sun in turbid water are not likely to affect miracidia. The miracidia survive better at moderate temperatures than at high or low ones, and apparently do not infect snails when the water temperature is below 10°C.[35] Miracidia remain infective for an average of 8 h in fresh water and have been shown to remain active for up to a maximum of about 20 h. On the average, miracidia survive 10.6 h.[79] Miracidia of S. haematobium are negatively phototactic and are affected positively by gravity.[92] They appear less sensitive (i.e., phototactic) to low-light intensity than do the miracidia of S. mansoni[92] (see discussion of S. mansoni phototaxis in section on Mode of Transmission of S. mansoni and S. japonicum).

The schistosome ova are the most resilient environmentally. Once excreted, schistosome eggs may survive for weeks or months, but they hatch promptly in water.[3] Schistosoma haematobium eggs cannot survive over 8 d in urine at room temperature.[3] They are known to remain viable for 2 d in experimental saline solutions, but have also been shown to survive longer in saline solutions (i.e., 1.75 to 2.5%) than in fresh water.[93] In salinities less than 8.5%, ova hatch generally within 1 h.[93] Under ideal environmental conditions, ova hatch within 18 h.[79] In studies performed in water from Lake Chilwa, Malawi, 89% of S. haematobium ova hatched within 3 h in daylight, but only 12% hatched in total darkness.[79] Turbid water and deoxygenation appear to retard hatching.[79] The optimum pH for survival of S. haematobium ova is between 7 and 8.[79] Also, the ova of S. haematobium are less tolerant to salt than are ova of S. mansoni[79]; the former are adversely affected by waters with a conductivity greater than 2000 µmho/cm, and are seriously affected at conductivities greater than 4000 µmho/cm.[79]

Persistence of S. haematobium is also affected by factors governing the survival and proliferation of their snail host. Snails and S. haematobium cercariae both increase in numbers in the early spring and summer,[69,91] and few of either snails or cercariae are found in winter, in excessively rainy periods, or in times of flood.[68,91] Snails may survive dry periods by estivation.[68]

The adult flukes have an average life span of 3.4 y, as reported from tests conducted in Gambia.[75] Other estimates of worm half-life range from 3 to 6 y. Schistosomes have been documented to survive up to 30 y, but the source of this information did not specify the species.[3] Typically, ova are discharged in urine for 5 y.[1]

DOSE RESPONSE ASSOCIATED WITH S. haematobium

The dose-response relationship for S. haematobium is not known at this time. Kloos et al.[69] reported an infection in Kloos that occurred after he swam in the Nile River for a total exposure period of 11.5 h, in an area thought to be safe from risk of infection. Levels of cercariae in the water were not reported; however, Upatham and Sturrock[94] reported that one S. mansoni cercaria per liter of water can produce infection. More research is needed on this topic.

LATENCY PERIOD FOR SCHISTOSOMIASIS PRODUCED BY S. haematobium

The prepatent period, that amount of time from infection to production of eggs by mature adults, is about 10 to 12 wk for S. haematobium.[2] The incubation period, the time between infection and onset of symptoms, is less clear. Symptoms frequently develop gradually or not at all,[3] but they may occur in primary infections 2 to 6 wk after exposure.[1]

DISINFECTION OF S. haematobium FROM WATER

Only a small amount of information has been gathered on disinfection of S. haematobium ova, miracidia, or cercariae. Chlorination is reported to easily remove cercariae (type and percent removed unspecified) from drinking water, as does storage for 2 d.[3]

Tables 6 and 7 show the effect of temperature and UV irradiation on S. haematobium miracidia. As shown, temperature and infective survival time are inversely related. Basically, as the temperature increases, the infective survival time is reduced. Review of Table 7 indicates that UV light is effective only within the upper few inches of water, demonstrating that sunlight has only a small effect on miracidia survival.

MONITORING METHODS FOR S. haematobium

One method of monitoring for S. haematobium can be achieved by collecting snails from (suspect) infected waterways by scooping[90] or using a pond net.[83] The snails can then be induced to shed cercariae by exposure to sunlight[91] or an artificial light source.[83] Cercariae shed in this manner can be fixed with 4% formalin and counted using a dissecting scope. Differentiation of cercariae into the different types can be achieved by (1) a starch-gel-electrophoresis method,[91] or by (2) infection studies. Infection studies can be performed by immersing hamsters in cercaria-bearing water, either in the laboratory[83] or in infected natural waters, and subsequently examining mature worms and the eggs that the worms produced.

Table 6. Effect of temperature on survival of S. haematobium and S. mansoni miracidia.[a]

Temperature (°C)	Infective survival time (h)
5–10	>9–12
19	17
18–22	9–12
25–30	9–12
35–38	6–9

[a] From Ref. 35.

Table 7. Effect of UV irradiation on survival of S. haematobium and S. mansoni miracidia.[a]

Water depth (cm)	Irradiation time (min)	Effect
2-4	3	All killed
7	3	Lethargic
7	5	All killed
10	5	Some killed
30	10	No effect
20	8	No effect

[a] From Ref. 35. Study performed in clear water; irradiation from 25 cm away.

Cercarial counts in the environment have not been made for S. haematobium, although some studies are reported to be in press at this writing.[69] Cercarial counts of water containing laboratory-raised and laboratory-released S. mansoni cercariae have been performed by Rowan's filtration method (as modified by Sandt[95]) and direct filtration.[69]

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP FOR S. haematobium

No indicator-organism/pathogen relationship has been developed for S. haematobium. Because this disease is associated with urine and not feces, an indicator-organism/pathogen relationship based on fecal microbial indicators would not be expected.

ENVIRONMENTAL CONCENTRATION OF S. haematobium

The presence of S. haematobium cercariae in snails has a seasonal distribution.[68,69,80,87,91] In Rhodesia, the presence of cercariae of S. haematobium and their transmission to humans is highest in spring and early summer and lowest in winter and during heavy rains.[91] It is estimated that 90% of the annual transmission in Nile Delta villages is between June and September.[69] Transmission in Mauritania is limited primarily to the dry season.[68]

In Zambia, the snail-infection rate was described as low, whereas the prevalence in humans was comparatively higher. For example, in school children the infection rate ranged from 3 to 68.4% of the population.[80] This information indicates that the snail-infection rate is not a good indicator for level of infection in a population.

Table 8 lists the total number of snails and percentage of infected snails collected in several studies. Table 9 displays snail density and the percentage of infected snails collected in six Egyptian villages.

One study conducted in Southern Rhodesia reported the shedding rates during different time periods (see Table 10). Two peak shedding periods were evident, both during the dry season, with the September-to-October peak occurring during the hottest time of the year. In general, the snail population increases during the dry season and decreases during the rainy season.[96] This pattern has been demonstrated in Liberia, Ghana, Nigeria, Gambia, and Sierra Leone, which all experience an increase in snail population during the dry season and a decrease during the rainy season.[78]

The ova excretion rate in humans is highly variable. Excretion rates are shown in Table 11. Although the majority of infected persons have low to moderate infection,[99] a certain number of the afflicted have heavy infections. Intensity of infection can be correlated with egg output from infected individuals and duration of water contact of the exposed population, especially in children and young adults.[63,73] The peak excretion time of day is around noon,[97] plus or minus 2 h.[91]

Table 8. Snails in the environment.

Area	No. snails collected	Infected (%)	Description	Ref.
Rhodesia	1000[a]	0.7	Cold, dry season	91
Rhodesia	5000[a]	1.6	Hot season	91
Rhodesia	3000[a]	0.7	Rainy season	91
Rhodesia	4200[a]	0.86	Warm, post rains	91
Liberia	2496[b]	10.3	Bulinus globosus	78
Liberia	0-22[c]	Not specified	Not reported	78
Rhodesia	Not reported	26.8[d]	B. globosus	96
Egypt	4312[e]	0.21	Not reported	74

[a] Snails per contact point; no further description given.

[b] Number of snails collected in a total of 164 water-contact sites.

[c] Number of snails per min per collector.

[d] Range of percent of infected snails found was 0 to 83%.

[e] Snails gathered every 100 to 200 m in waterways. Each point covered by four sweeps with net; total area per point = 6 m^2.

Table 9. Density and percentage of infected Bulinus truncatus snails collected from six villages in Upper Egypt.[a]

Egyptian village	No. infected/ no. collected May	No. infected/ no. collected June	Ratio of no. infected (%) to total sampled March through June		Snail density in June (no./m^2)
Ghawasa	1/245	0/139	1/688	(0.15)	2.1 ± 1.8
Aulad Amir	0/48	5/70	5/229	(2.18)	5.8 ± 0.6
Gabalaw	0/73	Not reported	0/143	(0.0)	2.7 ± 2.0
Bugdadi	Not reported	2/1599	2/1599	(0.13)	27.0 ± 20.6
El Tod	0/695	1/947	1/1642	(0.06)	25.6 ± 18.8
Hanadi	Not reported	0/11	0/11	(0.0)	0.6 ± 0.4
Total	1/1061	8/2760	9/4312	(0.21)	Not reported

[a] From Ref. 74.

Table 10. Shedding rates for Schistosoma haematobium in Southern Rhodesia.[a]

Time period	No. cercariae/snail
April-June	91-502
July-September	0
September-October	170-342

[a] From Ref. 96.

Table 11. Rates of ova excretion in urine of human populations.

Area	No. of ova excreted per 10 mL urine	Average no. of ova excreted per 10 mL urine	Description of exposed population	Ref.
Egypt	1-399	50.7	School children	60
Sudan	0-3724	39.5	Schoolboys	97
N. Nigeria	1-1024	17.3	Boys	65
Egypt/Nile	0.10-3960	9.8-19.4	Students, age 5-16	69
Nigeria		435	Students, age 6-15	67
Liberia		13.2	General population	78
Kenya[a]	0 - >1000	212	School children	63
S. Egypt		48.1 ± 9.5		74
Upper Egypt	1-99		61.7% of infected	74
Upper Egypt		100-399	18.9% of infected	74
Upper Egypt		400 +	19.4% of infected	74
Gambia		113	Children, age 5	98
Gambia		651	Children, age 8	98
Gambia		179	Children, age 11	98
Gambia		14	Youth, age 16	98
Gambia		1.4	Adults, age 28	98
Gambia		0.68	Adults, age 43	98
Gambia		0.93	Adults, age 58	98
Gambia		118	Overall average	98
E. Sierra Leone	1-13	9 ± 3		85

[a] 47.1% of these Kenyan school children had egg counts of 50 ova/10 mL or less of urine.

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CHAPTER 13. HELMINTHS THAT CAUSE SCHISTOSOME DERMATITIS: Trichobilharzia, Gigantobilharzia, and Austrobilharzia

ETIOLOGY AND CLINICAL DISEASE

Schistosome dermatitis is an acute, noncommunicable, cutaneous, foreign-body reaction to penetration of the skin by those schistosome cercariae (free-swimming larvae) from nonhuman hosts. The cercariae enter the skin but cannot progress further; they are thereby destroyed, producing a sensitivity dermatitis.[1-4] Other names used to describe the condition are swimmer's itch, cercarial dermatitis, clam-digger's itch, sea-bather's itch, and paddy itch.[2,5] Species of the trematodes Trichobilharzia, Gigantobilharzia, and Austrobilharzia, normally parasites of birds, are known to be important causes of schistosome dermatitis.[6]

Dermal response to penetration by avian or mammalian cercariae begins with a brief (generally <1 h), relatively mild itching or prickling sensation at the time the cercariae enter the skin. Sites of cercarial entry may become reddened, and in about 10 to 15 h they develop into papules, producing an intense itching. The reaction may be exacerbated by scratching or rubbing. Severely affected areas may become swollen and edematous. By the second or third day, the papules become vesicles, which are often ruptured by scratching. The lesions generally heal and disappear about a week after infection, sometimes leaving a temporary darkening of the skin. The itching becomes intermittent and disappears after 5 to 10 d.[3,4,7,8]

Secondary bacterial infection may occur, particularly in cases of intense scratching and skin injury.[8] No internal complications have been found in the United States,[9] nor has any complication been reported elsewhere.

Schistosome dermatitis is a sensitization phenomenon. The first few exposures may have either a mild reaction or no skin reaction at all. Subsequent exposures can lead to severe skin reaction.[8] An immune reaction develops against the cercaria, both as it enters the skin live, and after it dies in the epithelial layers of the skin; generally, this immunity occurs within 24 h of entry.[8,9] In a few instances, cercariae have penetrated to deeper tissues. In highly sensitized persons, even small numbers of cercariae can cause very intense skin reactions.[8]

Diagnosis of schistosome dermatitis usually is positive for those persons with a history of contact with water during a previous 96-h period, and who possess a cutaneous rash found only in areas that came in contact with the water in question. Biopsies of papules may yield cercariae, although this is generally done only for scientific studies.[8] Sometimes serologic or skin tests for human schistosomiasis may be positive. Patients should not be treated for human schistosomiasis unless live eggs are found.[4,10]

Schistosome dermatitis treatment is symptomatic.[8,11] Antihistamines and antipruritic drugs have been used to relieve itching.[6] Treatment frequently is made to prevent secondary infection.[8] Prevention is brought about most effectively by molluscicidng affected areas (see a further discussion in the Disinfection section of this chapter). Brisk rubbing of the skin with a rough towel can help prevent cercarial entry, thus preventing the skin reaction after exposure.[6,8] Avoiding exposure to water infected with cercariae is the most effective protective measure. Application of a thick coating of vaseline or 41% dimethyl phthalate in a lanolin cream base to exposed skin areas is reported to be effective in preventing the development of schistosome dermatitis.[8] Clothing also appears to protect the skin.[8,12]

OCCURRENCE

Schistosome dermatitis probably has a worldwide distribution[8]; it has been noted particularly in the United States, Canada, Malaysia, and Japan. It has also been reported in Burma, India, Australia, New Zealand, Great Britain, France, Switzerland, Germany, Iran, Haiti, Cuba, El Salvador, and Mexico. The only reported cases in Africa come from the Transvaal region of South Africa, although schistosome dermatitis is believed to occur throughout the African continent. There have been no reports from South America.[8,12,13]

Several areas have reported schistosome dermatitis in the United States. The most heavily affected area is the North Central lake region. The affliction appears to be most prominent in populations located in Michigan, Wisconsin, and Minnesota.[8] Other areas where schistosome dermatitis has been reported include North Dakota, Illinois, Nebraska, Texas. Florida, Washington, Oregon, California, Nevada, Oklahoma, Connecticut, Rhode Island, New York, and Iowa.[6,8,14] Some evidence exists of higher incidence in areas located beneath major avian flyways.[1,9]

Young people, 5 to 9 y old, are affected more frequently than adults.[5,12] This is attributed typically to their increased duration of water exposure and their tendency to stay in shallow areas near the shore where cercariae concentrate.[7,9] Both sexes are affected with equal frequency.

Schistosome dermatitis usually is a recreational disease of bathers. However, it is an occupational disease among rice-field and paddy workers and rice farmers in Malaysia and Japan.[8] Biologists who collect fish, aquatic snails, or aquatic insects also may be at greater risk.[8] Clam diggers are occasionally affected, because schistosome dermatitis has resulted from exposure to salt water as well as fresh water.[8] Duck hunters and fishermen have been known to be affected.

Schistosome dermatitis has a seasonal distribution in temperate areas. The cercariae have a peak incidence in the U.S. during the warm months, frequently around July.[8,10] In the Great Lakes area, snails shed cercariae on bright, warm, sunny days in early to midsummer. However, shedding of cercariae has been reported as late as November in Michigan.[7] The peak periods of cercariae presence often coincide with peak vacationing and, hence, recreational water contact.[6,8] Daily peaks of cercarial output from snails vary, depending on species, from early morning until night.[6,8,12] Other factors can also cause wide fluctuations in cercariae numbers and irregularities in disease outbreaks; these factors are not well understood.[6]

There are few reported attack rates (i.e., rates of new cases) for schistosome dermatitis, or estimates of numbers of persons affected. Attack rates in several small outbreaks at the Swan Estuary, Perth, Western Australia, ranged from 0.8 to 25%.[12] An outbreak of schistosome dermatitis occurred among members of a biology field trip in Michigan in 1976; 55 4% of the participating students and instructors were afflicted.[1]

RESERVOIR

Two types of reservoir exist for schistosome dermatitis agents: a snail host and a vertebrate host. The snail host is the intermediate reservoir, harboring the larval form that can infect humans; humans are the abnormal vertebrate host.[3] Any of several species of the snail genera, including Lymnaea, Physa, and Stagnicola, can be this intermediate host.[8]

The definitive hosts of schistosome dermatitis are numerous. They include various waterfowl such as ducks and gulls, and other birds such as canaries, pigeons, blackbirds, starlings, and sparrows.[8,9,11,12] Mammals known to be reservoirs for this schistosome include cattle, muskrats, deer mice, and other small animals.[8]

MODE OF TRANSMISSION

Schistosome dermatitis is caused by the penetration of human skin by cercariae in search of a definitive host.[1,6,8,12] In the normal life cycle, the definitive host excretes eggs in the feces. When these eggs come in contact with water, they hatch to miracidia that seek and invade appropriate snail intermediate hosts. Inside the snail, they develop into cercariae, multiplying during this process. Cercariae break out of the snail and enter the skin of the definitive host, where they develop into adults and complete the cycle by producing eggs.[1,3,4,6]

SUSCEPTIBILITY AND RESISTANCE

Susceptibility of schistosome dermatitis is not well understood. Some people are repeatedly exposed with little or no effect, whereas others have increasingly severe reactions, necessitating avoidance of infected waters.[6,8] The speed of the response, which may take several exposures to initiate, tends to increase with increased exposure.[9]

ENVIRONMENTAL PERSISTENCE

Information on persistence of cercariae causing schistosome dermatitis is scarce. These cercariae can survive in the laboratory for 24 h, and in some cases for 2 to 3 d.[8] They can live for up to 24 h in the skin, and the bodies of dead cercariae may remain in the skin for 40 h.[10] Free-swimming miracidia in search of a snail host, can live for 6 to 12 h in water.[9,10] The parasite can live for months or sometimes years in both the snail and the definitive vertebrate hosts.[6]

The cercariae that produce schistosome dermatitis are known to penetrate the skin at temperatures from 17 to 23.5°C.[8] Many outbreaks of infection coincide with heat spells that are preceded by a period of much cooler weather. Low temperatures appear to inhibit cercarial escape from snails, although the cercariae may emerge in reduced numbers at temperatures as low as 9°C in the presence of light.[8]

DOSE RESPONSE

The dose-response relationship has not been determined for schistosome dermatitis. It is known that 30 to 90 min is the general period of water-exposure time required for infection.[12] In one study of infection, 400 <u>Cercaria</u> <u>stagnicola</u> were placed in 8 L of water contained in a bucket. Exposure of a 3-in.-wide section of forearm for 30 min at a water temperature of 19 to 22°C resulted in 39 lesions.[8]

LATENCY

The stinging sensation associated with schistosome dermatitis may be felt within 30 to 60 min after exposure, followed by reddening and maculation (discoloration of patches of skin). In persons who have been previously sensitized, papules appear in 10 to 20 h. Unsensitized persons may develop papules (pimples) with little or no itching 5 to 14 d after cercarial penetration.[3]

DISINFECTION

The use of disinfection for schistosome dermatitis control is directed toward eliminating snails from various waters. This can be done by applying molluscicides or removing vegetation.[4] Copper sulfate appears to be used most frequently.[8,14] The dose commonly recommended is 2 lb $CuSO_4$ per 1000 ft^2 of bottom area.[14] Sometimes it is necessary to treat only part of a water body, such as a designated swimming area and its environs.[14] Copper sulfate treatment has been reported to be effective over a period of several months to 3 y.[14] Optimal control is achieved by two treatments, 4 to 6 wk apart, in the early spring.[14]

Cercariae succumb to 1 ppm iodine in 30 min. Chlorination is also reported to kill cercariae, as does heat (temperature not specified).[2]

MONITORING METHODS

No monitoring methods have been established for detecting the presence in water of the cercariae that are responsible for producing schistosome dermatitis.

INDICATOR-ORGANISM/PATHOGEN RELATIONSHIP

There is no indicator-organism/pathogen relationship for the cercariae causing schistosome dermatitis. Observation of the presence of aquatic snails and ducks indicates the potential for schistosome dermatitis.[11]

ENVIRONMENTAL CONCENTRATION

No information is available on the concentration of the cercariae that produce schistosome dermatitis in the environment.

Complicating the acquisition of such data are the facts that the numbers of cercariae emerging from one snail may be in the thousands,[6] and the timing of snail and cercarial maturation and shedding is associated directly with light and with water temperature.[1]

Table 1. Percentage of snails in various regions infected with cercariae that can produce schistosome dermatitis in exposed humans.

Area	Percentage of infected snails (%)	Ref.
Lake Bemidji, MN	12.3	8
Lake Shinji, Japan	5	8
La Jolla, CA	1–4.5	8
Coronado Island, Mexico	1–4.5	8
Shadow Cliffs Lake, CA	1.7	14
Perth, W. Australia	9	12

However, some environmental data do exist. For example, in Swan Estuary, Perth, Western Australia, 9% of snails were found to be infected with cercariae of Australobilharzia terrigalensis. Gulls in this area released 1 to 46 schistosome ova per pellet of feces; 76.9% (10 of 13) of these birds were found to be infected.[12]

Table 1 lists the percentage of infected snails reported in a variety of locations. It would appear that in most cases, the percentage of snails infected with dermatitis-producing cercariae is less than or equal to 5%.[8]

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CHAPTER 14. RISK ASSESSMENT

INTRODUCTION

The task of assessing health risks associated with the pathogens listed in Table 1 involves many factors, and the existing body of scientific knowledge on the subject varies from essentially zero (speculative) to well-established facts. Unfortunately, as presented in previous chapters, much of the information is speculative. Because of the lack of data, the risk-assessment approach presented here is semiquantitative and limited to the presentation of an environmental classification scheme that allows for the relative comparison of pathogens, based on their potential health risks and control strategies.

The evaluation of the health risks posed by these pathogens and the identification and efficacy of control strategies require information in the following three main categories: (1) the presence of the agents that cause disease, (2) the dose-response characteristics of the agents, and (3) the probable mode of contact between the agent and susceptible individuals. These categories can be defined further to include information on pathogen concentration, latency, infectivity, persistence, infective dose, and reservoirs. A discussion of each of these areas follows, along with a presentation of the available data for the pathogens listed in Table 1.

PATHOGEN CONCENTRATION

Estimates of the concentration of pathogens in surface waters are summarized in Table 2. As shown, only a small amount of data is available. Simple estimates of the concentrations in sewage are difficult to make because data on the prevalence of infection in a specific region of a country and the volume of related sewage are not available. Also, estimates of the concentration of many of the helminth pathogens (i.e., schistosomes) are difficult to make because helminths do not complete multiplication within the definitive invertebrate host. Thus, the data that are available will be used to illustrate the magnitude of the potential health hazard that individuals may encounter.

LATENCY

The term "latency" is defined as the time interval between infection and the onset of symptoms. Review of the data shown in Table 3 indicates that the latency period for

Table 1. Water-related pathogens selected for review.

Bacteria	Protozoa	Helminths
Non-cholerae Vibrio spp.	Acanthamoeba spp.	Dracunculus medinensis
Pseudomonas spp.	Naegleria spp.	Ascaris lumbricoides
Staphylococcus spp.	Balantidium spp.	Schistosoma spp.
Leptospira spp.		Trichobilharzia spp.
Aeromonas spp.		Gigantobilharzia spp.
		Austrobilharzia spp.

the bacteria and protozoa categories of pathogens is typically a few days and generally less than 10 d. Latency periods for the helminths is significantly longer, on the order of weeks and months.

INFECTIVITY

Infectivity is defined as the interval between the excretion of a pathogen and its infection of a new host. As shown in Table 3, the pathogens in the bacteria and protozoa categories are infective immediately. The helminth infections, however, generally all have a noninfective period.

ENVIRONMENTAL PERSISTENCE

Persistence of the organism in the environment is a measure of how quickly it dies after leaving the human host. A summary of available data on persistence is shown in Table 3. A pathogen with a short persistence time outside the host is more likely to be transferred person to person. Personal cleanliness, then, becomes an important factor relative to the transmission of pathogens with short environmental persistence. A pathogen with a relatively long persistence time in the environment is more likely to be transferred between human hosts by other means (i.e., water). Control measures, which include providing a treated-water supply and minimizing contact with raw water (i.e., lakes, ponds, etc.), are important in limiting the transmission of these pathogens.

Table 2. Concentration of water-related pathogens in sewage and water.

Pathogen	Organisms/L of sewage: Developed countries	Organisms/L of sewage: Undeveloped countries	Organisms/L of fresh water: Developed countries	Organisms/L of fresh water: Undeveloped countries
Bacteria:				
Non-cholerae *Vibrio* spp.	?	?	?[a]	?
Pseudomonas spp.	10^6 [b]	?	3×10^3 [c]	?
Staphylococcus spp.	2×10^4 [b]	?	60[c]	?
Leptospira spp.	3×10^3 [b]	?	10[c]	?
Aeromonas spp.	?	?	4×10^4 [d]	?
Protozoa:				
Acanthamoeba spp.	?	?	?	?
Naegleria spp.	?	?	?	?
Balantidium spp.	?	?	?	?
Helminths:				
Dracunculus medinensis	?	?	?	2[d]
Ascaris lumbricoides	30–100[d]	600[e]	<1[c]	4[c]
Schistosoma:				
S. haematobium	?	1[e]	?	?
S. japonicum	?	10[e]	?	?
S. mansoni	?	120[e]	?	?
S. mekongi	?	?	?	?
Schistosome (trematode) cercariae	?	?	?	?

[a] Marine environment.

[b] Ref. 1.

[c] Estimate based on 10% of organisms reaching surface waters; 1:10 dilution.

[d] Literature review related to this report.

[e] Ref. 2.

Table 3. Basic features of excreted pathogens.

Pathogen	Time intervals: Latency	Infectivity	Environmental persistence	Median infective dose (ID_{50})[a]
Bacteria:				
Non-cholerae Vibrio spp.	?	0	?	With wound, high; without wound, very high
Pseudomonas spp.	2 d	0	>30 d	With wound, high; without wound, very high
Staphylococcus spp.	<1 d	0	?	Low-high
Leptospira spp.	7-10 d	0	1 wk to 7 months	Low
Aeromonas spp.	1 d	0	Hours to weeks	With wound, medium; without wound, very high
Protozoa:				
Acanthamoeba spp.	>7 d	0	Very long	Medium
Naegleria spp.	3-7 d	0	>42 d	Medium
Balantidium spp.	Few d	0	Weeks[b]	Low
Helminths:				
Dracunculus medinensis	10-14 months	2-6 wk	4-7 d to few months	Low
Ascaris lumbricoides	Few days to months	10 d	1 y	Low
Schistosoma spp.[c]	4 to 6 wk	4 to 7 wk	2 d	Low
Schistosome (trematode) cercariae	<1 d	4 to 7 wk	2 d	Low

[a] Median infective dose (organisms): low = $<10^2$; medium = 10^4; high = $>10^6$.

[b] Only for cysts of Balantidium spp.

[c] Includes S. haematobium, S. japonicum, S. mansoni, S. mekongi.

INFECTIVE DOSE

The median infective dose (ID_{50}) is used here as a gauge of pathogen infectivity and thus allows for a comparison between pathogens. As shown in Table 3, information is limited, relative to the doses required to infect half of the exposed population. The ID_{50} values shown in Table 3 are estimates based on human and/or animal data and in some cases "expert opinion" found in our literature review.

Review of the data indicates that a wide range of infective doses exists. For some pathogens, the infective dose is a few organisms (e.g., Leptospira spp.: $<10^2$ organisms), whereas for others it is high (e.g., Pseudomonas spp.: $>10^6$ organisms). Generally, the estimates for bacterial infections, with or without wounds, indicate that the infective dose is on the order of 10^4 to 10^6 organisms. For the helminth infections, a single egg or larva can infect if ingested, even though the worms may fail to mature.[2]

RESERVOIR

As shown in Table 4, some diseases are almost exclusively infections of man. However, many of the pathogens listed in Table 4 involve animals as alternative hosts or as hosts for other stages in the organisms' life cycle. Because animals are a major reservoir for many of these pathogens, the proper collection, treatment, and disposal of waste, alone, will not provide the necessary controls to eliminate the transmission of disease associated with these pathogens.

COMMON MODE OF TRANSMISSION

Review of Table 4 indicates that generally the mode of transmission for the pathogens under review either is through person-to-person contact or is by direct contact of skin with contaminated water and/or soil. The two exceptions are for the pathogens Balantidium coli and Dracunculus medinensis, where transmission is achieved primarily through the ingestion of contaminated water. Following the classification scheme of Feachem[2] and Bradley,[3] these pathogens can be classified as either water-washed or water-based.

CLASSIFICATION OF EXCRETION-RELATED INFECTIONS

Following the work done by Feachem[2] and Bradley,[3] five environmental categories of infection (as shown in Table 5), can be defined for the pathogens under review. These

Table 4. Selected water-related pathogens: summary of reservoir and mode of transmission.

Pathogen	Reservoir[a]	Common mode of transmission
Bacteria:		
Non-cholerae Vibrio spp.	Human	Water (D),[b] person-to-person
Pseudomonas spp.	Human, animal	Water (D), person-to-person
Staphylococcus spp.	Human	Water (D), person-to-person
Leptospira spp.	Human, animal	Water (D), soil
Aeromonas spp.	Soil	Water (D), moist soil
Protozoa:		
Acanthamoeba spp.	Water, soil, and fish	Water (D), soil, freshwater fish
Naegleria spp.	Water and soil	Water (D), soil, freshwater fish
Balantidium spp.	Animal	Water (I)[c]
Helminths:		
Dracunculus medinensis	Human and possibly animal	Water (I,D)
Ascaris lumbricoides	Human, animal	Soil, food, water (D)
Schistosoma spp.	Human, snail	Water (D)
Schistosome (trematode) cercariae	Animal, snail	Water (D)

[a] Definitive host.

[b] D = transmission by direct contact of skin with soil and/or water containing organism.

[c] I = transmission by ingestion of water containing organism.

categories are based on the environmental features previously discussed, which include latency, infectivity, infective dose, and mode of transmission. Control measures appropriate to each category also are shown in Table 5. These environmental categories of infection can be defined as follows:

Table 5. Environmental classification of excreted infections.

	Environmental category	Selected organisms	Infection	Mode of transmission	Major control measure
I.	Immediately infective, low infective dose, short latent period	Balantidium	Balantidiasis	Water (ingested), person-to-person contact	Treated-water supply[a]
II.	Immediately infective, medium or high infective dose, moderately persistent, short latent period	Naegleria	Skin and eye meningoencephalitis	Person to person, water (contact), soil contact	Health education, treated-water supply,[a] limit contact with water
III.	Immediately infective, low infective dose, persist..., animal host, moderate latent period	Leptospira spp.	Leptospirosis	Water (contact), person to person, soil contact	Limit contact with water, health education, treated-water supply[a]
IV.	Not immediately infective, low infective dose, moderately persistent, no intermediate host, long latent period	Ascariasis lumbricoides	Ascariasis	Person to person, soil, water contact	Health education, provision of toilets, treated-water supply[a]
V.	Not immediately infective, low infective dose, persistent, aquatic intermediate host, long latent period	Schistosoma spp., et al.	Schistosomiasis, dracontiasis, cercarial dermatitis	Water contact	Limit contact with water, treated-water supply,[a] control of intermediate host, improved sanitation (e.g., toilets), health education

[a] Treatment could be provided by a reverse osmosis water-purification unit (ROWPU).

Category I. The infections in this category have a low infective dose ($<10^2$ organisms ingested), are infective immediately upon excretion, and can be spread easily whenever water supplies are untreated and personal hygiene is not ideal. However, ingestion of water containing the organisms is required.

Category II. The infections in this category have a medium or high infective dose, are infective immediately upon excretion, and can be spread easily from person to person whenever water supplies are untreated and personal hygiene is not ideal. In addition, contact with untreated water (i.e., lakes, ponds) is associated with the transmission of these pathogens.

Category III. The infections in this category are similar, in terms of their environmental classification, to those in Categories I and II, except for one important difference. These organisms require an animal host as part of their life cycle. Also, limiting host contact with untreated water (i.e., lakes, ponds) is a significant factor in controlling these infections.

Category IV. The infections in this category have a low infective dose and are not immediately infective upon excretion. This category contains the soil-transmitted helminths. Provisions for the proper collection, treatment, and disposal of wastes and personal hygiene are important control measures for this category.

Category V. The organisms in this category are water-based helminths that require an aquatic host to complete their life cycles. Control is achieved by limiting host contact with untreated water (i.e., lakes, ponds, standing water), the provision of a treated-water supply (in the case of dracontiasis), and the control of the intermediate host.

A definite difference exists between the first two categories and the last three. For example, the last three categories require an animal host or intermediate aquatic host as part of the mode of transmission. Also, for the last three categories, the major control measures involve limiting contact between the potential host and untreated water (i.e., ponds, lakes, standing water) and providing toilets rather than a treated-water supply.

Table 5 presents complementary methods for controlling an infection. For example, if a treated-water supply is provided, independent of other control methods, the likely effectiveness of complementary control measures for each category would be as follows:

Category I: excellent
Category II: slight to moderate
Category III: negligible
Category IV: negligible
Category V: negligible for schistosomiasis; excellent for dracontiasis.

RISK-ASSESSMENT SUMMARY

As previously discussed, the assessment of risk posed by these pathogens is semiquantitative and limited to the presentation of an environmental classification that allows for the comparison of pathogens and associated control strategies. The pathogens were classified (as shown in Table 5) into five environmental categories. These categories allow for a comparison between pathogens based on key pathogen characteristics such as infectivity, persistence, and infective dose. Based on this type of classification, the immediate risk posed to military personnel is the highest from pathogens in Category I and the lowest from pathogens in Category V. However, if the assumption is made that all of these organisms will be present within water and also immediately infective, it would be more realistic to base the comparison of risk of infection on median infective dose of the pathogen and its latency. This assumption results in the comparison of organisms as shown in Table 6. Review of Table 6 indicates that the pathogens can be roughly grouped as follows: short latency (i.e., <7 d) and low infective dose (i.e., $<10^2$ organisms), long latency and low infective dose, and short latency and medium-to-high infective dose. Based on this type of classification, it appears that the pathogens that present the highest risk of infection, relative to a short latency period (i.e., <7 d), appear to be Staphylococcus spp., Leptospira spp., Balantidium coli, and Ascaris lumbricoides. The next group of pathogens that present the highest risk of infection, relative to the long latency period (i.e., 1 y) appear to be Schistosoma spp. and Dracunculus medinensis. The final group of pathogens is the group with a medium-to-high infective dose and a short latency period. Unless the concentration of these pathogens in water is quite high, it appears that they present the lowest risk of infection.

The previous discussion focused on the risk of infection, assuming no treatment of the water supply. If a treated-water supply is provided, the likely effectiveness of controlling disease from each of the environmental categories would be as follows:

Group I: slight
Group II: negligible for schistosomiasis, excellent for dracontiasis
Group III: slight to moderate.

Table 6. Grouping of pathogens based on latency and infective dose.

Pathogen	Latency (time interval)	Median infective dose[a]
Group I:		
Staphylococcus spp.	< 1 d	Low to high
Leptospira spp.	< 7 d	Low
Balantidium coli	Few d	Low
Ascaris lumbricoides	Few d to several months	Low
Group II:		
Schistosoma spp.	4 to 6 wk or longer	Low
Cercarial dermatitis	4 to 6 wk or longer	Low
Dracunculus medinensis	10 to 14 mo	Low
Group III:		
Acanthamoeba spp.	> 7 d	Medium
Naegleria spp.	3 to 7 d	Medium
Non-cholerae Vibrio spp.	?	Medium to high
Pseudomonas spp.	2 d	Medium to high
Aeromonas spp.	1 d	High

[a] Median infective dose (organisms ingested and/or adsorbed; see Table 4): low $\leq 10^2$; medium=10^4; high $\geq 10^6$.

The provision of a treated-water supply, in combination with an adequate supply of water and limiting the contact of personnel with untreated water (i.e., lakes, ponds, rivers), should adequately control the transmission of the above pathogens.

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CHAPTER 15. UNCERTAINTIES AND RESEARCH RECOMMENDATIONS

During the process of gathering and reviewing information on the disease organisms listed in Table 1 of Chapter 1 and Table 1 of Chapter 14, it became apparent that several areas of information needed further research. Table 1 of this chapter presents a summary of the key areas where insufficient or no information is available, thereby identifying data gaps and potential areas for future research. A review of Table 1 for bacterial organisms indicates the following:

1. For the more recently identified etiologic agents of water-washed, water-based disease organisms reviewed in this text, such as Aeromonas spp. and non-cholerae Vibrio spp., all categories of research need to be explored or improved. No adequate enumeration techniques or monitoring methods exist; the fate or role of these organisms in the environment is not well defined; and the effectiveness of disinfectants in the control of these agents should be studied further. Although the clinical symptomology and pathogenicity of these organisms have recently been described, few studies have addressed the parameters of dose response, latency, or immunity.

2. Information on the other bacterial pathogens reviewed (i.e., Staphylococcus spp., Leptospira spp., Pseudomonas spp.) is generally available in some detail but needs better definition so that quantitative estimates of health risks can be computed. Clinically, much information has been collected on these organisms, because they have been of major concern for many years. Areas such as occurrence and carrier rates, concentration in raw water, and secondary attack rates still need to be better defined.

3. One of the most important but neglected areas is the relationship between indicator-organisms and pathogens. Frequently, the correlation between coliform numbers in water and numbers of pathogens or the disease rate in those exposed to contaminated water is complicated and incomplete. It was also noted that a serious question exists as to the advisability of using coliforms as indicators of water quality in tropical areas of the world. Research is needed to (a) demonstrate which microorganism(s) would best serve as indicators of water quality under a variety of conditions; (b) determine the relationship between indicator-organisms and the numbers of specific infectious organisms that may be present; and (c) develop methods for the rapid detection and enumeration, in water, of appropriate indicators for specific pathogens or for the pathogens themselves. These data are essential to improving the confidence of disease-risk estimates based on water-quality criteria.

Table 1. Summary of key areas of uncertainty for water-based and water-washed organisms.[a]

Key: (-) = a small amount to no data, data base needed; (+) limited data, needs improvement; (++) adequate data available.

Organism	Occurrence in water	Dose response	Latency	Environmental persistence	Disinfection	Monitoring methods	Indicator-pathogen	Environmental concentration
Aeromonas spp.	+	+	++	+	+	+	-	+
Leptospira spp.	+	+	++	+	+	+	-	-
Pseudomonas spp.	+	-	++	+	++	++	+	+
Staphylococcus spp.	+	+	+	+	++	++	-	+
Non-cholerae Vibrio spp.	-	-	-	+	+	+	-	+
Acanthamoeba spp.	-	-	-	-	+	+	-	-
Balantidium coli	-	-	-	-	-	-	-	-
Naegleria spp.	-	-	+	+	++	+	-	-
Ascaris lumbricoides	+	+	++	++	+	-	-	++
Dracunculus medinensis	+	+	++	-	-	+	-	+
Schistosoma haematobium	+	-	+	+	+	+	-	+
S. mansoni	+	-	+	+	+	+	-	+
S. japonicum	+	-	+	+	-	+	-	+
S. mekongi	+	-	+	-	-	-	-	-
Schistosome (trematode) cercariae	+	-	++	-	+	-	-	-

[a] Schistosome (trematode) cercariae are free-swimming larvae that produce a sensitivity dermatitis referred to as swimmer's itch, cercarial dermatitis, and other descriptive names.

4. Limited information is available concerning the survival of bacterial pathogens in water under various environmental conditions (pH, temperature, salinity, organic loading, effect of indigenous microflora, etc.). Data concerning the environmental concentration of bacterial pathogens in water systems are generally inadequate and therefore need collecting. Additional research is needed to monitor seasonal or annual fluctuations of organisms in water and the impact of rural, suburban, and urban areas on bacterial pathogen concentrations and survival rates.

A review of Table 1 for protozoal pathogens indicates the following:

1. Only a small amount of information is available with regard to (1) human dose-response relationships, (2) occurrence and concentration in water, and (3) indicator-organism/pathogen relationships. Additional research should be conducted in these areas to improve understanding with regard to these organisms and to allow for quantitative estimates of risk.

2. Reliable information is needed for the above-mentioned protozoal parasites concerning their survival rates in water, before, during, and after water treatment.

A review of Table 1 for the helminths indicates the following:

1. Only a small amount of information is available with regard to (1) human dose-response relationships, (2) occurrence and concentration in water, and (3) indicator-organism/pathogen relationships. Additional research should be conducted in these areas to improve understanding with regard to these organisms and to allow for quantitative estimates of risk.

2. Reliable information is needed for the previously mentioned helminths concerning their survival rates in water, before, during, and after water treatment.

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